Challenging Cases in Lung SBRT

April 22, 2021

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INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER
Conquering Thoracic Cancers Worldwide

CME ACCREDITED

Challenging Cases in Lung SBRT

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Publications

Coming Soon in the JTO:

Stereotactic Radiation for Lung Cancer: A Practical Approach to Challenging Scenarios

Neal Andruska, MD, PhD; Hayley B. Stowe, MD; Cathryn Crockett, MBBCH, BAO, MRCP, FRCR; Wei Liu, MD; David Palma, MD; Corinne Faivre-Finn, FRCR, MD, PhD; Shahed N. Badiyan, MD

Additional publications:

A Primer on Interstitial Lung Disease and Thoracic Radiation

Brief Report on Radiological Changes following Stereotactic Ablative Radiotherapy (SABR) for Early-Stage Lung Tumors: A Pictorial Essay

Stereotactic Body Radiation Therapy for Central Early-Stage NSCLC: Results of a Prospective Phase I/II Trial

Radiosensitivity of Lung Metastases by Primary Histology and Implications for Stereotactic Body Radiation Therapy Using the Genomically Adjusted Radiation Dose

Biologically Effective Dose in Stereotactic Body Radiotherapy and Survival for Patients with Early-Stage NSCLC

Disclosures

- **Corinne Faivre-Finn, FRCR MD PhD** discloses she receives research funding from Astra Zeneca, MSD Pharmaceuticals and Elekta and is on an advisory board and scientific committees for Astra Zeneca.
- **David Palma, MD, PhD, FRCPC** has no relevant financial relationships to disclose.
- **Shahed Badiyan, MD** discloses he receives speaker's honoraria from MEVION Medical Systems.

All other planners, reviewers and staff reported no relevant financial relationships.

All relevant financial relationships have been mitigated.

Ultra-central Early Stage Non-Small Cell Lung Cancer

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Polling Question 1

Which of the following is the most common source of high grade toxicity in patients treated with hypofractionated radiation/SBRT for ultra-central early stage non-small cell lung cancer?

A. Chest wall toxicity

B. Spinal cord myelitis

C. Pulmonary hemorrhage

D. Pericarditis

Case Presentation

- 78 year old male underwent annual chest CT for surveillance of a left lung nodule found years earlier after a motor vehicle collision.

- Medical History:
  - 30 pack-year smoking history. Quit 30 years ago.
    - FEV1= 98% predicted (3.9 L)
    - DLCO = 74% predicted

- Chest CT: New 2.8 cm mass in superior RLL. Stable LLL nodule.

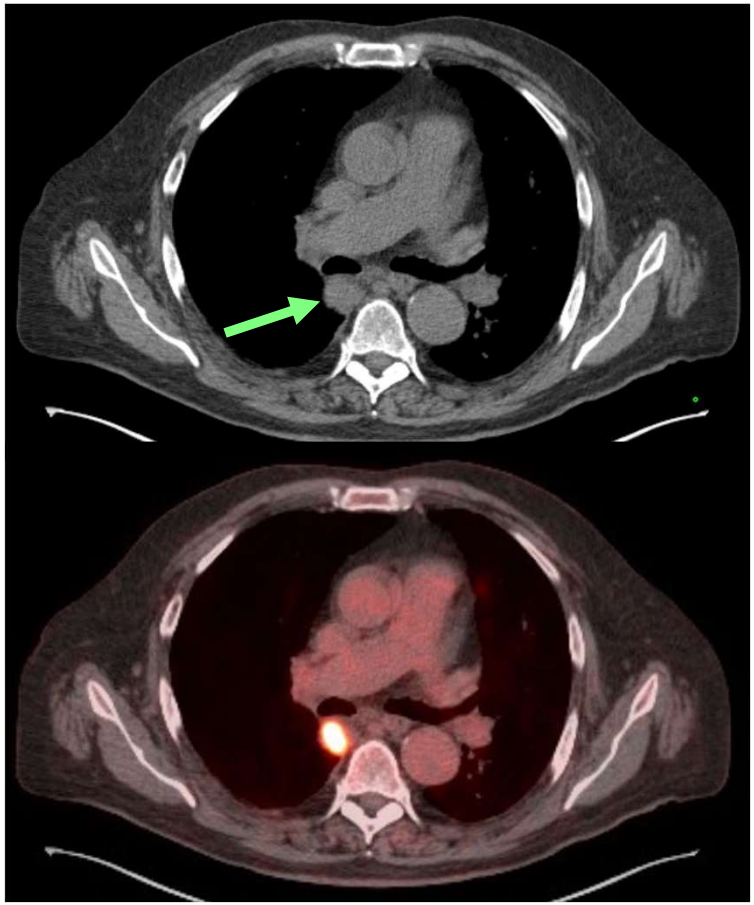
Workup

CT Chest:

- Right lower lobe azygo-esophageal recess mass, 2.8 cm, abutting right main stem bronchus
- No lymphadenopathy

PET/CT Scan:

- Right lower lobe azygo-esophageal recess hypermetabolic lesion, SUVmax 21.4
- No FDG avid lymphadenopathy
- No distant metastases



Tissue Diagnosis and Staging

- Flexible Bronchoscopy:
  - No endobronchial tumor seen

- EBUS for mediastinal staging:
  - No visibly enlarged nodes
  - EBUS transbronchial FNA of RLL mass:
  - Pathology: poorly differentiated NSCLC, favor squamous cell carcinoma

Case: Our Patient's Treatment

- **What would you recommend?**

- Offered RLL superior segmentectomy by thoracic surgeon
- Repeat bronchoscopy in OR by surgeon found extrinsic compression of right mainstem bronchus without frank invasion.
- Surgery aborted due to likelihood of needing pneumonectomy or complex reconstruction of airway

- Patient referred for SBRT

Common Dose Options

- Central:
  - 50-55 Gy in 5 Fx (common in the U.S.)
  - 60 Gy in 8 Fx (common in Canada / Europe)
  - 48 Gy in 4 Fx
  - 60 Gy in 5 Fx (MTD as per RTOG 0813)

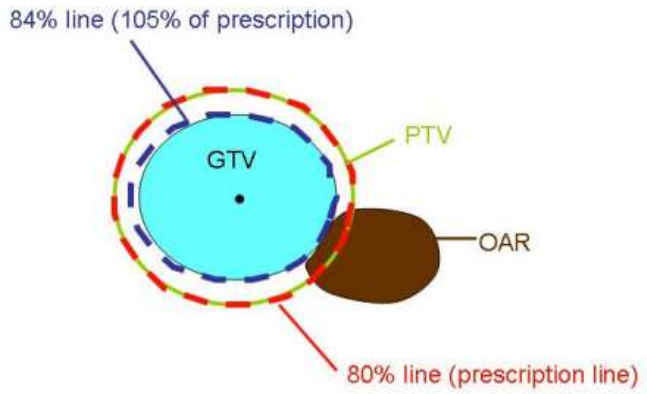
- Ultracentral:
  - 60 Gy in 8 Fx
  - 50 Gy in 5 Fx
  - 60 Gy in 12 Fx
  - 60 Gy in 15 Fx
  - Conventional RT

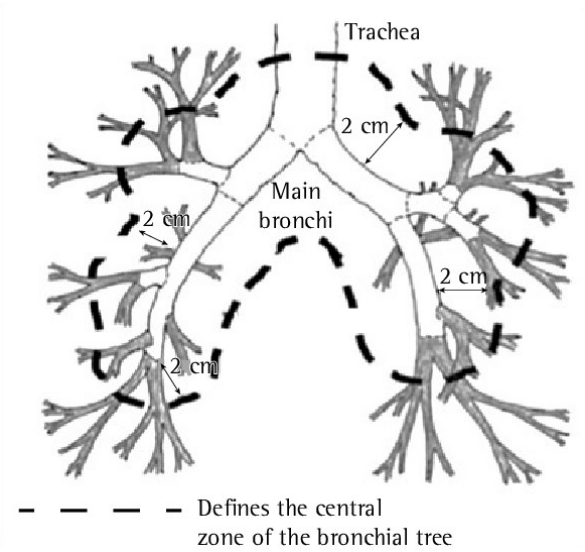
RTOG 0813

IASLC

Safety and Efficacy of a Five-Fraction Stereotactic Body Radiotherapy Schedule for Centrally Located Non–Small-Cell Lung Cancer: NRG Oncology/RTOG 0813 Trial

Andrea Bezjak, MD[1]; Rebecca Paulus[2]; Laurie E. Gaspar, MD[3]; Robert D. Timmerman, MD[4]; William L. Straube, MS[5]; William F. Ryan, MD[6]; Yolanda I. Garces, MD[7]; Anthony T. Pu, MD[8]; Anurag K. Singh, MD[9]; Gregory M. Videtic, MD[10]; Ronald C. McGarry, MD, PhD[11]; Puneeth Iyengar, MD, PhD[4]; Jason R. Pantarotto, MD[12]; James J. Urbanic, MD[13]; Alexander Y. Sun, MD[1]; Megan E. Daly, MD[14]; Inga S. Grills, MD[15]; Paul Sperduto, MD[16]; Daniel P. Normolle, PhD[17]; Jeffrey D. Bradley, MD[5]; and Hak Choy, MD[4]





Bezjak A, et al. J Clin Oncol. 2019 May 20;37(15):1316-1325.

TABLE A2. Dose Limits Indices as Specified in the Protocol: Organs at Risk

Tissue	Volume (mL)	Volume Max, Gy (Gy/fx)	Max Point Dose, Gy (Gy/fx)	Avoidance End Point
Serial				
Spinal cord	< 0.25	22.5 (4.5)	30 (6)	Myelitis
	< 0.5	13.5 (2.7)		
Ipsilateral brachial plexus	< 3	30 (6)	32 (6.4)	Neuropathy
Skin	< 10	30 (6)	32 (6.4)	Ulceration
Parallel*				
Lung (right and left side)	1,500	12.5 (2.5)		Basic lung function
Lung (right and left side)	1,000	13.5 (2.7		Pneumonitis
Serial				
Esophagus, nonadjacent wall	< 5	27.5 (5.5)	105†	Stenosis/fistula
Heart/pericardium	< 15	32 (6.4)	105†	Pericarditis
Great vessels, nonadjacent wall	< 10	47 (9.4)	105†	Aneurysm
Trachea and ipsilateral bronchus, nonadjacent wall	< 4	18 (3.6)	105†	Stenosis/fistula

Abbreviations: fx, fraction; Max, maximum.
*Listed are critical volume and critical volume dose maximum.
†Percentage of planning target volume (PTV) prescription.

Bezjak A, et al. J Clin Oncol. 2019 May 20;37(15):1316-1325.

Ultra-central Definitions and Outcomes

Study	Definition of Ultra-central	Dose/Fractionation	2-yr Local Control	Toxicity
HILUS Phase II, 2021 (n=65)	≤ 1 cm from PBT	56 Gy/8 fx (100%) 150% hotspot	83%	Grade 3+: 34% Grade 5: 15%
Breen, 2021 (n=110)	GTV abutting PBT, trachea; PTV overlap PBT, trachea; GTV ≤ 1 cm from PBT	50 Gy/5 fx (57%) 60 Gy/8 fx (15%) 48 Gy/4 fx (13%)	84%	Grade 5 (4%)
RTOG 0813, 2019 (n=120)	≤ 2cm from PBT	50-60 Gy/5 fx	87.9-89.4%	7.2% DLTs
Raman, 2018 (n=26)	PTV overlapping PBT, trachea, esophagus, pulmonary vein/artery	60 Gy/8 fx (77%) 50 Gy/10 fx (12%)	100%	Grade 2-3: 7.9% Grade 4-5: 0%
Tekatli, 2016 (n=47)	PTV overlapping trachea or main bronchi	60 Gy/12 fx 140% hotspot	78%	Grade 3+: 38% Grade 5: 13%
Li, 2014 (n=82)	Dose constraints for 50 Gy in 4 fx not met	70 Gy/10 fx (100%)	96.2%	Grade 3: 3.6% Grade 5: 1.2%

Tekatli H, et al. J Thorac Oncol. 2016 Jul;11(7):1081-9.
Lindberg K, et al.. J Thorac Oncol. 2021 April 3. Epub.
Li et al. Radiother Oncol. 2014 Aug;112(2):256-261

Breen WG, et al. Radiother Oncol. 2021 Mar 10;158:246-252.
Bezjak A, et al. J Clin Oncol. 2019 May 20;37(15):1316-1325.
Raman S, et al. Clin Lung Cancer 2018 Sep;19(5):e803-e810

Systematic Review

ELSEVIER

Journal of Thoracic Oncology

Available online 7 May 2019

In Press, Corrected Proof

Original Article

Safety and Effectiveness of Stereotactic Ablative Radiotherapy for Ultra-Central Lung Lesions: A Systematic Review

Hanbo Chen MD [a], Joanna M. Laba MD [a], Sondos Zayed MD [a], R. Gabriel Boldt MLIS [a], David A. Palma MD, PhD [a], Alexander V. Louie MD, PhD [b]

CAUTION

- High doses to PBT
- Endobronchial disease
- Bevacizumab or anticoagulants

Current Trial: SUNSET

- Multicenter phase I dose-finding study
- Starting dose: 60 Gy in 8 fx. Hot spot limited to 120%
- Ultracentral definition: PTV touches or overlaps the central bronchial tree, esophagus, pulmonary vein, or pulmonary artery

Giuliani et al, Clin lung cancer 2018

SUNSET Schema

Patients with ultra-central NSCLC

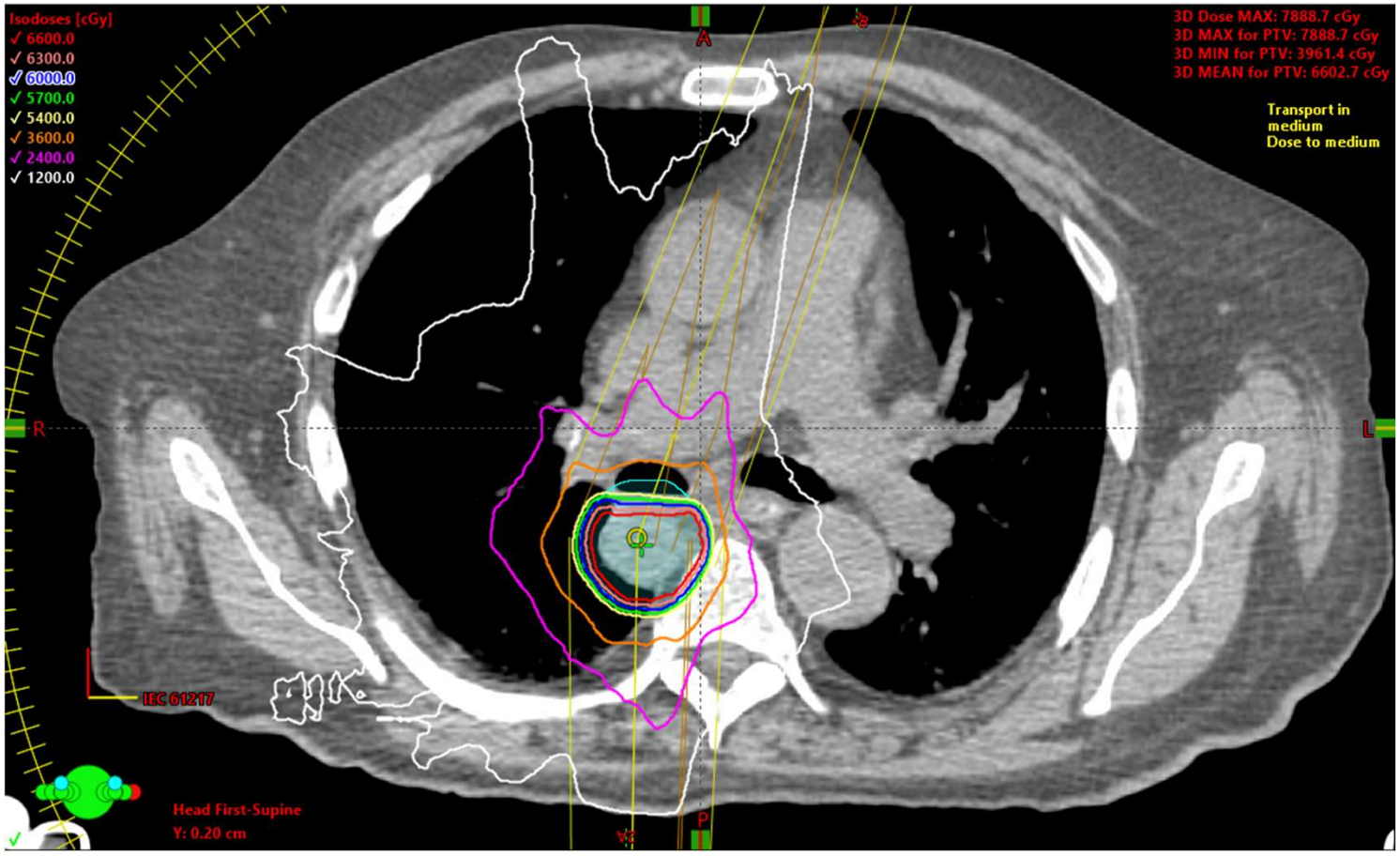
T1-3 (≤6 cm) N0 M0

DOSE LEVELS

	Level -1	Level 0	Level 1	Level 2	Level 3
Dose per fraction:	4 Gy	6 Gy	7.5 Gy	10 Gy	12 Gy
Number of fractions:	15	10	8	6	5
Total Dose:	60 Gy	60 Gy	60 Gy	60 Gy	60 Gy

Giuliani et al, Clin lung cancer 2018

Patient Plan



60 Gy in 12 fx

VMAT 2 arcs:
20-181 degrees Clockwise
& Counter clockwise

Hot spot of 35%

Dose Constraints

Table 2 Recommended Dose Constraints

Organ	Metric	Fraction		
		5/6	8/10	15
Spinal canal	Max	30 Gy	32 Gy	39.5 Gy
Spinal canal PRV (3 mm)	Max	32 Gy	34 Gy	42 Gy
Esophagus	Max	40 Gy	45 Gy	50.5 Gy
	5 cc	35 Gy	40 Gy	48 Gy
Brachial plexus	Max	32 Gy	39 Gy	50 Gy
Heart	Max	62 Gy	64 Gy	66 Gy
	10 cc	50 Gy	60 Gy	62 Gy
Trachea	Max	62 Gy	64 Gy	66 Gy
	10 cc	50 Gy	60 Gy	62 Gy
Proximal bronchus	Max	62 Gy	64 Gy	66 Gy
	10 cc	50 Gy	60 Gy	62 Gy
Non-GTV lung	Mean	< 12 Gy	< 12 Gy	< 14 Gy
Aorta and major vessels	Max	62 Gy	64 Gy	64 Gy
	10 cc	50 Gy	60 Gy	60 Gy
Stomach and intestines	Max	40 Gy	45 Gy	50 Gy
	10 cc	35 Gy	40 Gy	48 Gy

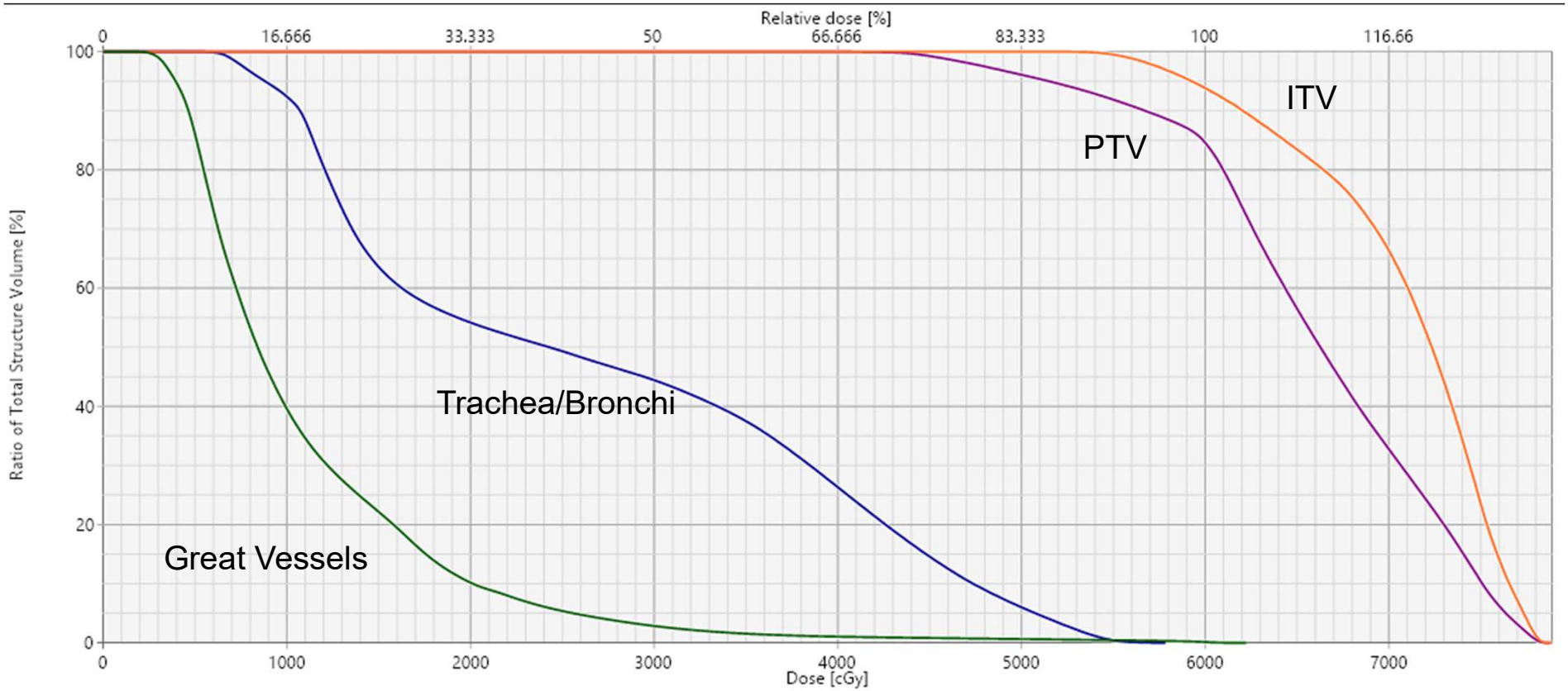
Abbreviations: GTV = gross tumor volume; PRV = planning organ-at-risk volume.

12 Fraction Regimen Dose Constraints

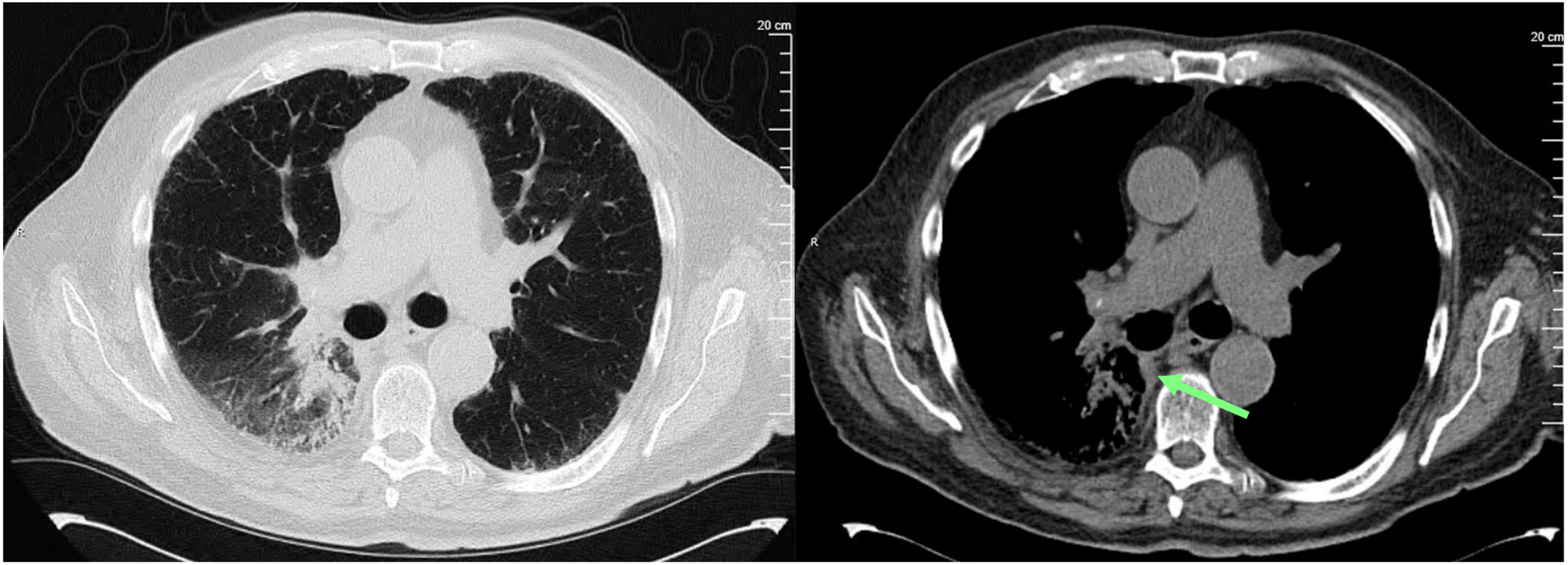
	Volumetric Constraint	Max point dose
Spinal cord	D0.35cc < 31.2 Gy	37.8 Gy
Esophagus	D5cc < 21.6 Gy	48 Gy
Trachea & Bronchi	D5cc < 52 Gy	59 Gy
Great Vessels	D10cc < 55.7 Gy	62.9 Gy
Heart	D15cc < 38.2 Gy	43.7 Gy

Giuliani et al, Clin lung cancer 2018

Patient Plan



3 month post-treatment CT



Key Points

- Ultra-central tumors require more caution
- Use dose constraints for great vessels, trachea/large bronchi
- Beware of high doses to the PBT, endobronchial invasion, and bevacizumab or anticoagulation
- Optimal doses and constraints will hopefully be determined soon!

Resources

- Chen H, et al. Safety and Effectiveness of Stereotactic Ablative Radiotherapy for Ultra-Central Lung Lesions: A Systematic Review. J Thorac Oncol 2019 Aug;14(8):1332-1342
- Guiliani M, et al. SUNSET: Stereotactic Radiation for Ultracentral Non-Small-Cell Lung Cancer-A Safety and Efficacy Trial. Clin Lung Cancer 2018 Jul;19(4):e529-e532.
- Tekatli H, et al. Outcomes of Hypofractionated High-Dose Radiotherapy in Poor-Risk Patients with "Ultracentral" Non-Small Cell Lung Cancer. J Thorac Oncol. 2016 Jul;11(7):1081-9.
- Lindberg K, et al. The HILUS-trial – a prospective Nordic multi-center phase II study of ultra-central lung tumors treated with stereotactic body radiotherapy. J Thorac Oncol. 2021 April 3. Epub. In press. https://doi.org/10.1016/j.jtho.2021.03.019.
- Breen WG, et al. Ablative radiotherapy for ultracentral lung cancers: Dosimetric, geometric, and volumetric predictors of outcomes and toxicity. Radiother Oncol. 2021 Mar 10;158:246-252.
- Bezjak A, et al. Safety and Efficacy of a Five-Fraction Stereotactic Body Radiotherapy Schedule for Centrally Located Non-Small-Cell Lung Cancer: NRG Oncology/RTOG 0813 Trial. J Clin Oncol. 2019 May 20;37(15):1316-1325.
- Raman S, et al. Ultracentral Tumors Treated With Stereotactic Body Radiotherapy: Single-Institution Experience. Clin Lung Cancer 2018 Sep;19(5):e803-e810
- Li Q, et al. Stereotactic ablative radiotherapy (SABR) using 70 Gy in 10 fractions for non-small cell lung cancer: Exploration of clinical indications. Radiother Oncol 2014 Aug 112(2):256-261.

Management of Multiple Lung Lesions

David Palma, MD, PhD, FRCPC
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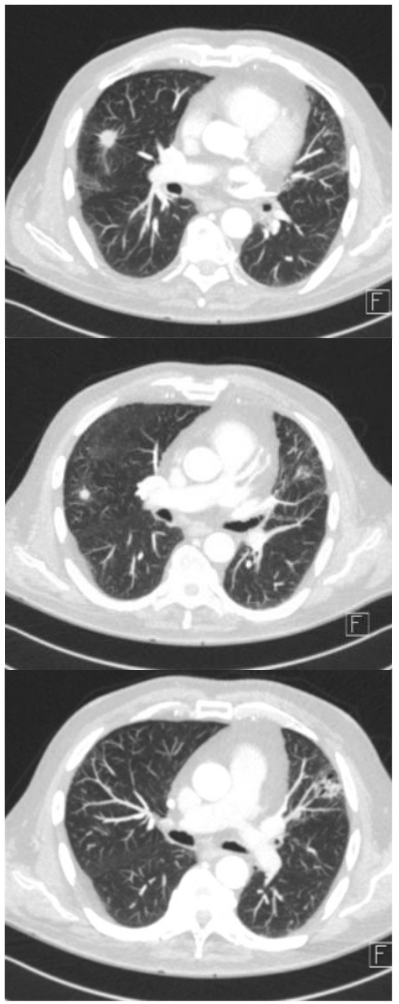
Case Presentation

- 85 year-old man with prior history of a T3N2c squamous cell carcinoma of the supraglottis treated with chemoradiation in 2010.

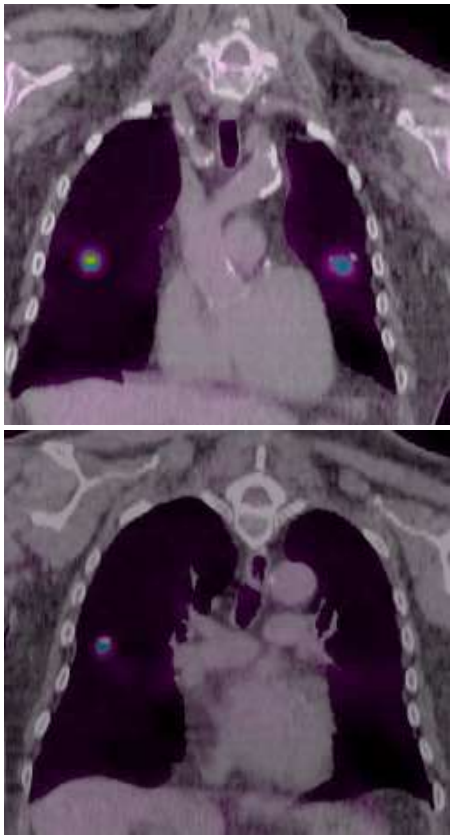
- Presented in May 2017 with a cough. CXR showed nodules in right lung and CT scan ordered.

- Three lesions, all new from 2010.



Case Presentation

- Medical History: Diabetes, angina, moderate COPD (80 pack years) – FEV1 = 55% predicted.
- Repeat CT 3 months later shows growth of all 3.
- PET-CT shows all three lesions have SUVmax between 6-9



Polling Question 2

In patients with multiple lung cancers detected on initial scan, with no prior scans, the lesions are most likely to be:

A. Synchronous primaries
B. One primary with two metastases
C. Two primaries with metastasis from one of them
D. Impossible to know

Polling Question 3

What would you recommend for this patient?

A. Observation
B. Resection of all lesions
C. Systemic therapy
D. SABR to all sites

Clinical Considerations

- Do we need a biopsy? If so, how many lesions do we biopsy?
- Are these multiple primaries or mets?
- Observation or Treatment? Which options?

One Primary or Multiple

The IASLC Lung Cancer Staging Project: Background Data and Proposed Criteria to Distinguish Separate Primary Lung Cancers from Metastatic Foci in Patients with Two Lung Tumors in the Forthcoming Eighth Edition of the TNM Classification for Lung Cancer

- *"It is easier to determine that two tumors are different than that they are the same; finding similarities does not establish that they are the same."*

Goldstraw P, Chansky K, Crowley J, et al. The IASLC Lung Cancer Staging Project: Proposals for Revision of the TNM Stage Groupings in the Forthcoming (Eighth) Edition of the TNM Classification for Lung Cancer. *J Thorac Oncol*. 2016;11(1):39-51. doi:10.1016/j.jtho.2015.09.009

ARTICLE

Received 25 Feb 2016 | Accepted 11 Sep 2016 | Published 21 Oct 2016 DOI: 10.1038/ncomms13200 OPEN

Genomic heterogeneity of multiple synchronous lung cancer

- Genomic profiles analyzed from 15 lung adenocarcinomas in 6 patients
- All suggested independent primary tumors (not metastases)

Liu Y, Zhang J, Li L, et al. Genomic heterogeneity of multiple synchronous lung cancer. *Nat Commun.* 2016;7:13200. Published 2016 Oct 21. doi:10.1038/ncomms13200

Table 2. Clinical Criteria for Separate versus Related Pulmonary Tumors

Clinical criteria[a]
Tumors may be considered separate primary tumors if
They are clearly of a different histologic type (e.g., squamous carcinoma and adenocarcinoma).
Tumors may be considered to be arising from a single tumor source if
Matching breakpoints are identified by comparative genomic hybridization.
Relative arguments that favor separate tumors:
Different radiographic appearance or metabolic uptake
Different pattern of biomarkers (driver gene mutations)
Different rates of growth (if previous imaging is available)
Absence of nodal or systemic metastases
Relative arguments that favor a single tumor source:
The same radiographic appearance
Similar growth patterns (if previous imaging is available)
Significant nodal or systemic metastases
The same biomarker pattern (and same histotype)

[a]Note that a comprehensive histologic assessment is not included in clinical staging, as it requires that the entire specimen has been resected.

Plan Evaluation: One Additional Parameter

COMMENTARY

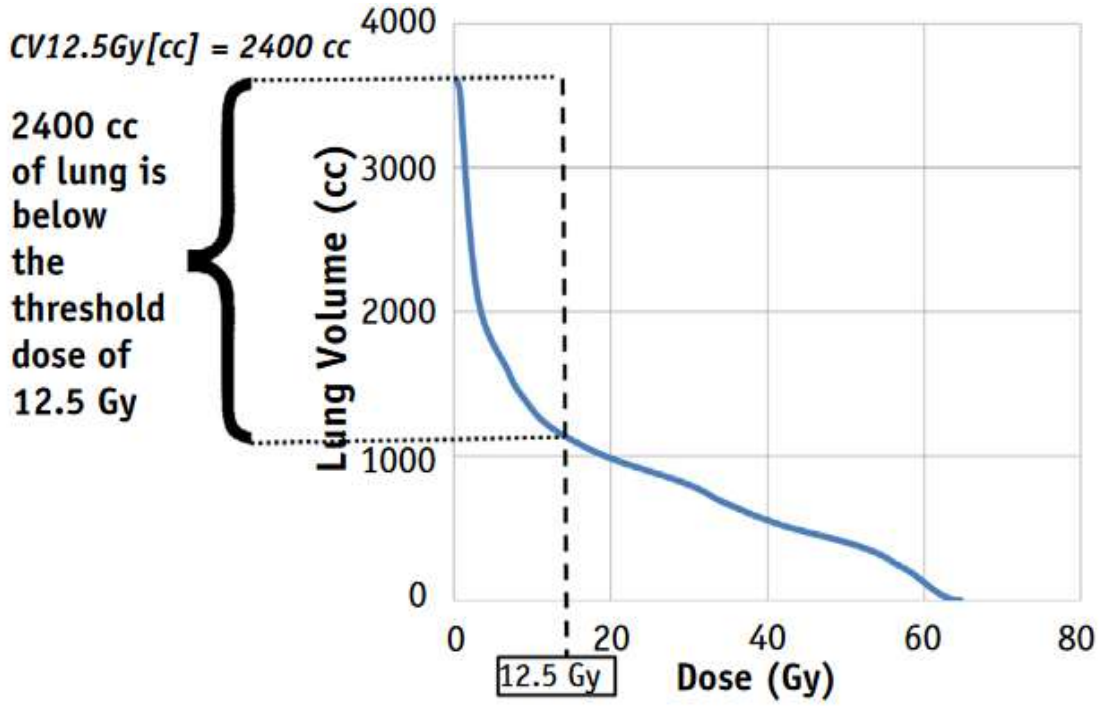
Application of Critical Volume-Dose Constraints for Stereotactic Body Radiation Therapy in NRG Radiation Therapy Trials

Timothy A. Ritter, PhD,*,†,†† Martha Matuszak, PhD,†,†† Indrin J. Chetty, PhD,‡,†† Charles S. Mayo, PhD,‡,†† Jackie Wu, PhD,§,†† Puneeth Iyengar, MD, PhD,‖,†† Michael Weldon, MS,¶,†† Clifford Robinson, MD,#,†† Ying Xiao, PhD,**,†† and Robert D. Timmerman, MD‖,††

CV12.5 = volume receiving 12.5 Gy or less

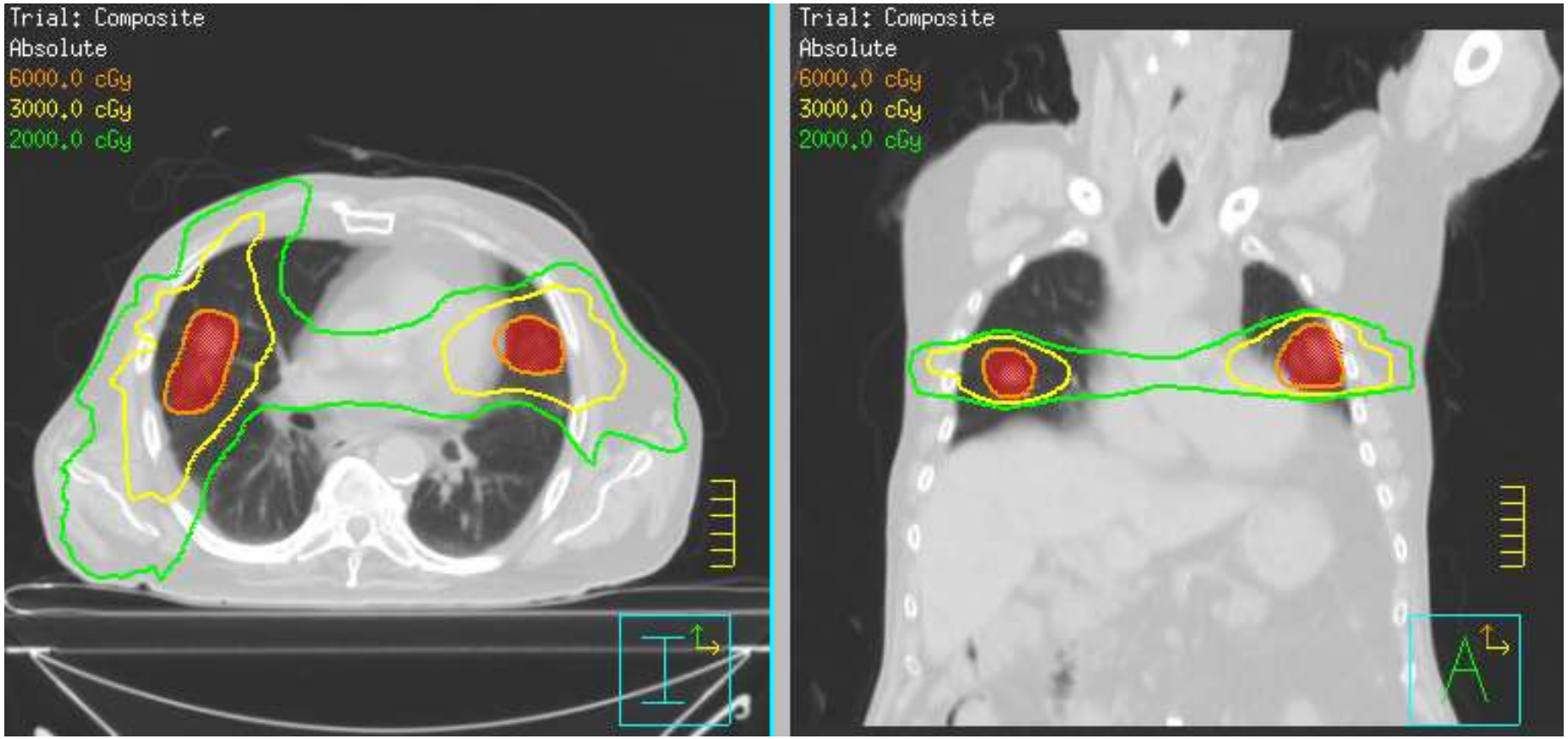
5 fraction constraint:

1.5 L receiving <12.5 Gy

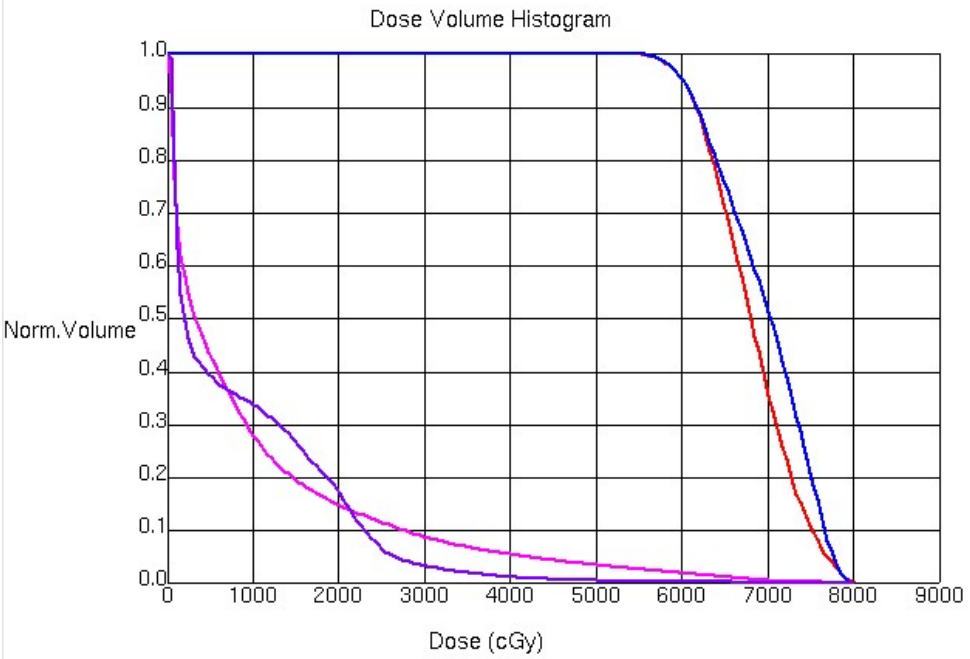


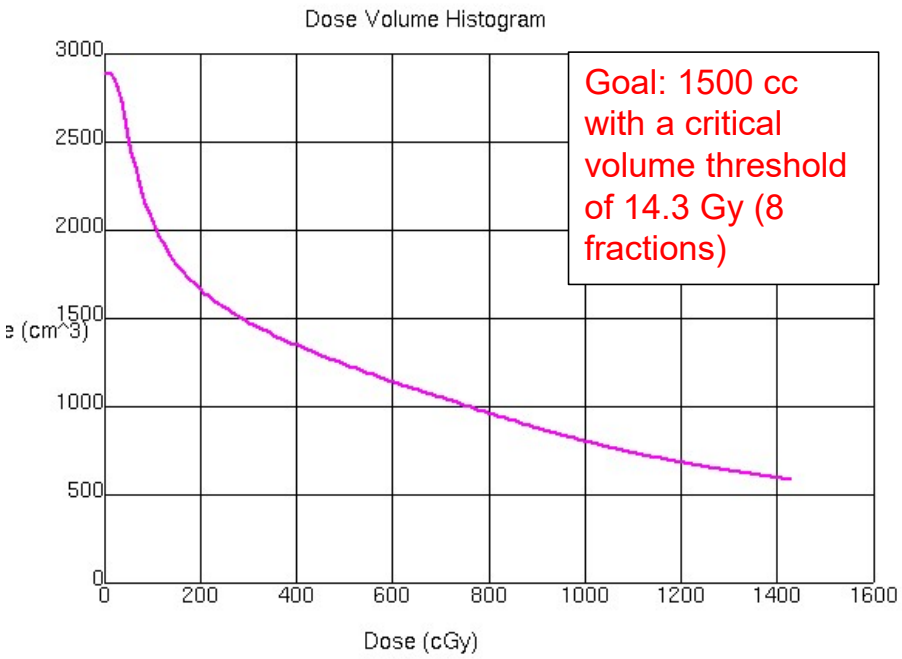
Ritter TA, Matuszak M, Chetty IJ, et al. Application of Critical Volume-Dose Constraints for Stereotactic Body Radiation Therapy in NRG Radiation Therapy Trials. Int J Radiat Oncol Biol Phys. 2017;98(1):34-36. doi:10.1016/j.ijrobp.2017.01.204

Our Case: 60 Gy in 8 fractions



DVH





Goal: 1500 cc with a critical volume threshold of 14.3 Gy (8 fractions)

Each PTV optimized separately. There was some contribution across plans, so each PTV was optimized to be under-covered; good coverage on composite plan

Key Points

- Synchronous lesions are most likely to be synchronous primaries (polling question #1)

- The best treatment is unknown and the approach should be individualized. Both surgery and SABR have advantages and disadvantages.

Re-SBRT of Lung Cancer

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Polling Question 4

Grade 3+ toxicity rates with re-SBRT for lung cancer are approximately:

A. 10%
B. 30%
C. 60%
D. 80%

Case Presentation

- 73 year old male underwent annual chest CT for surveillance for surveillance of pulmonary nodules 3 years prior

- Medical History:
  - 40 pack-year smoking history. Continues to smoke 5 cig/day
  - Colon cancer, T3N1M0, 4 years prior, s/p hemicolectomy and FOLFOX x 6 cycles
  - Type II DM on insulin
  - COPD

- Chest CT: New 9 mm LUL spiculated nodule. No lymphadenopathy

Workup

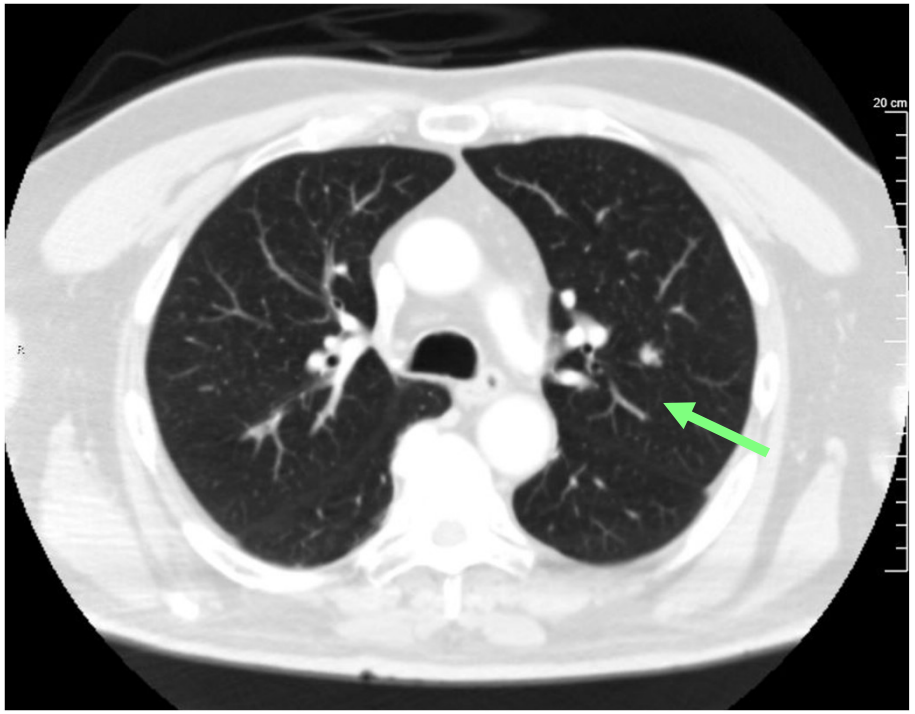
CT Chest:

- LUL 9 mm spiculated nodule
- No lymphadenopathy

PET/CT Scan:

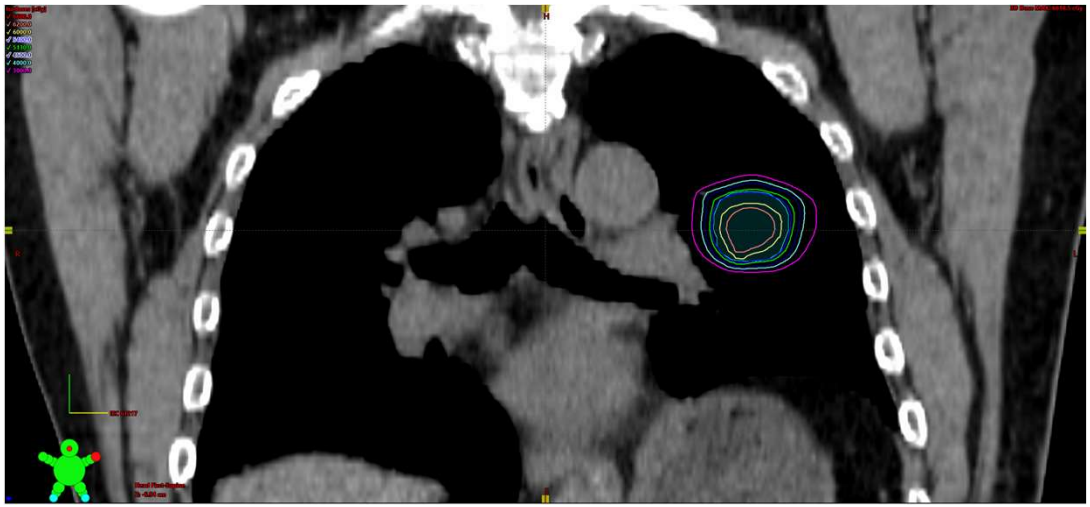
- LUL nodule SUV max 1.7. Other nodules not FDG avid.
- No FDG avid lymphadenopathy
- No distant metastases

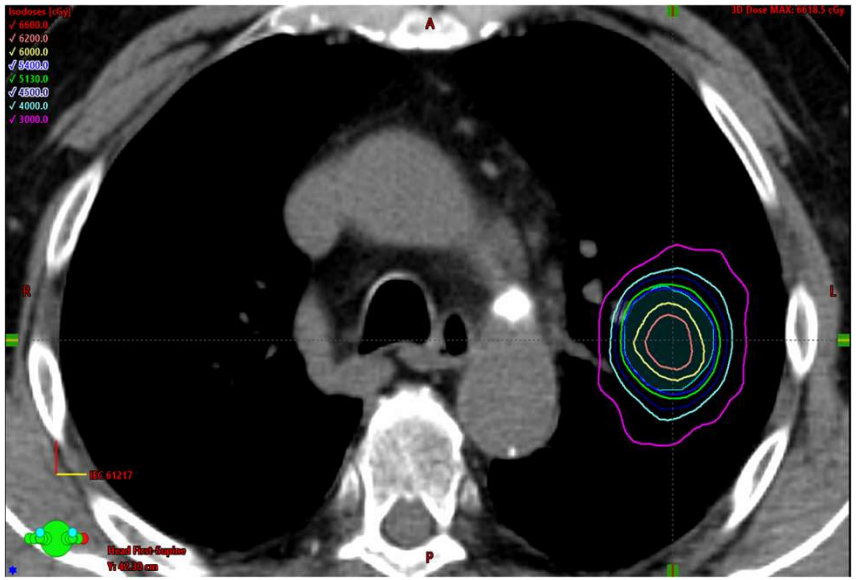
- **EBUS:**
  - No visibly enlarged nodes
  - EBUS transbronchial FNA of LUL nodule
  - Pathology: moderately differentiated adenocarcinoma, TTF-1 +, likely lung primary



Case: First Treatment

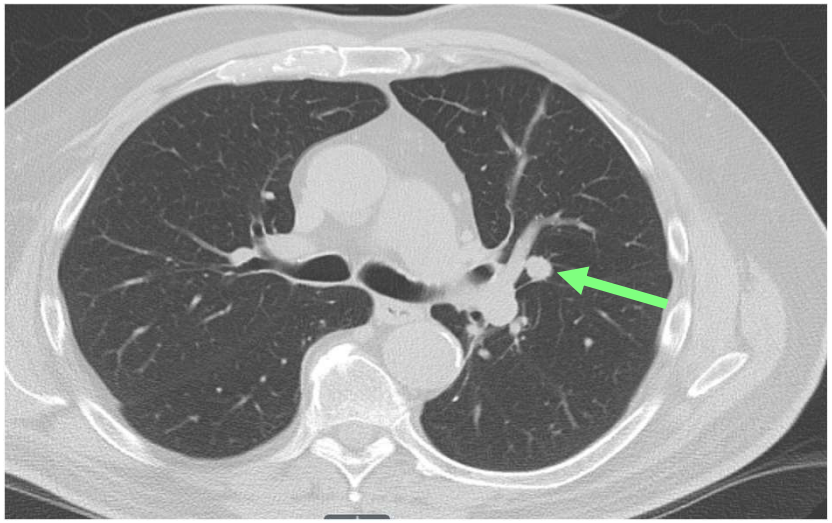
- Patient referred for SBRT
- Received 54 Gy in 3 fx every other day
  - 7 field FFF plan

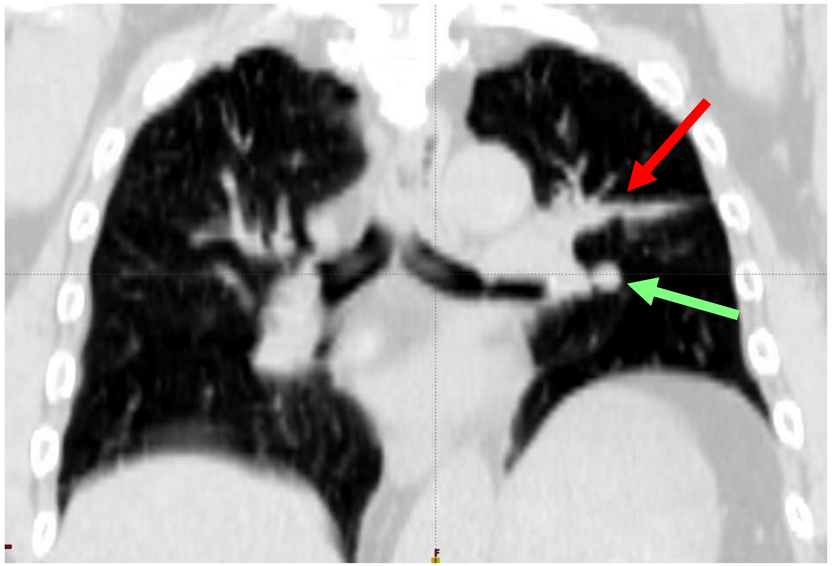




Case: Patient Follow-up

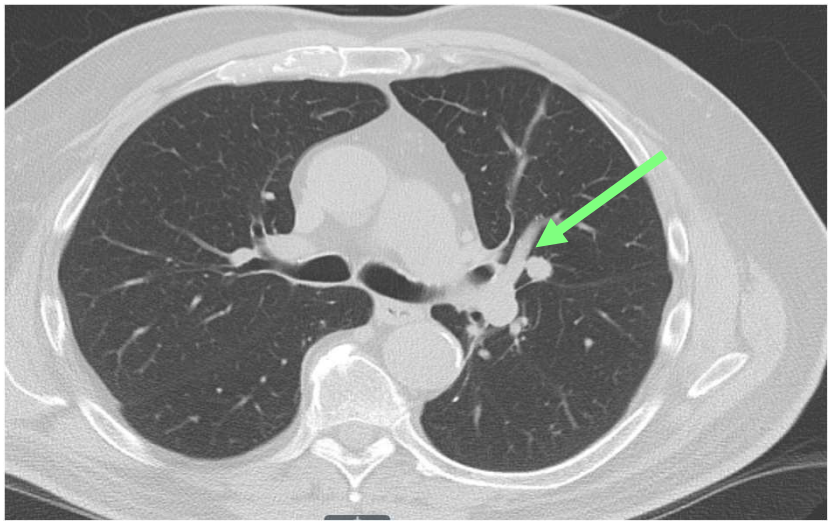
- Did well for 2.5 years
- CT chest showed growth of LUL nodule (now 13 mm) inferior to radiation fibrosis.
- PET/CT: LUL nodule inferior to radiation fibrosis has SUVmax of 4.2





Case: Metachronous NSCLC in prior SBRT field

- Recommendation at Multi-D Tumor Board:
  - No biopsy due to location
  - Not a good surgical candidate
  - Recommend SBRT



Re-SBRT Definitions and Outcomes

Study	Definition of Re-SBRT	Dose for re-SBRT	Local control outcomes	Toxicity
Kennedy et al. 2020 (n=21)	Within 1 cm of PTV or overlap of ≥ 25% isodose lines	50 Gy/5 fx (57%) 54 Gy/3 fx (43%)	2-yr 81%	Gr 2 pneumonitis: 10% Gr 2 chest wall: 19% Gr 3+: 0%
Hearn et al. 2014 (n=10)	Marginal failures within 1 cm of PTV	50 Gy/ 5 fx (70%) 60 Gy/ 3 fx (30%)	60%	Gr 1-2 fatigue: 30% Gr 1-2 chest wall: 50% Gr 3+: 0%
Peulen et al. 2011 (n=29)	>50% overlap of PTVs	30 Gy / 2 fx (34%) 40 Gy/ 5 fx (28%) 45 Gy/ 3 fx (21%)	5 mo 52%	Gr 3-4: 28% Gr 5 hemorrhage: 10%

Kennedy WR, et al. Radioth Oncol 2020

Heart J, et a. Int J Radiat Oncol Biol Phys 2014

Peulen H, et al. Radioth Oncol 2011

Re-SBRT Meta-analysis

ORIGINAL ARTICLE

Effectiveness and Safety of Reirradiation With Stereotactic Ablative Radiotherapy of Lung Cancer After a First Course of Thoracic Radiation

A Meta-analysis

Gustavo A. Viani, MD, PhD, Caio V. Arruda, MS,† and Ligia I. De Fendi, MD‡*

- Re-SBRT for 625 lung lesions in 595 patients
- 86% primary lung cancer
- 51% First course RT conventional fx
- 45% central recurrence
- 2-year LC 73%
- 2-year OS 54%
- Grade 3+ toxicity: 9.8%
  - Pneumonitis most common
- Grade 5: 1.5%

Viani et al Am J Clin Oncol 2020

Re-SBRT Meta-analysis

- LC associated with:
  - Re-SBRT dose (p=0.034)
  - Tumor size (p=0.04)
- Cumulative dose >145 Gy2:
  - 15% risk of Grade 3+ toxicity
- Cumulative dose <145 Gy2
  - 3% risk of Grade 3+ toxicity

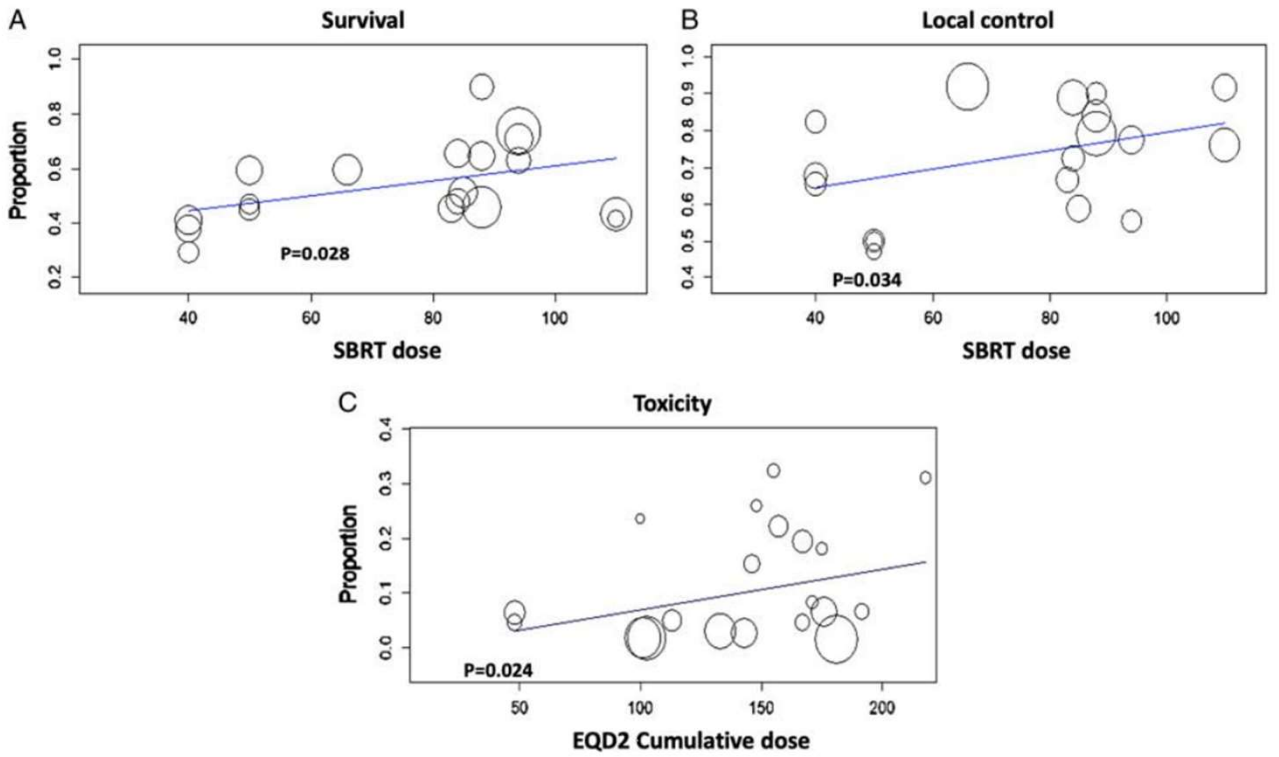
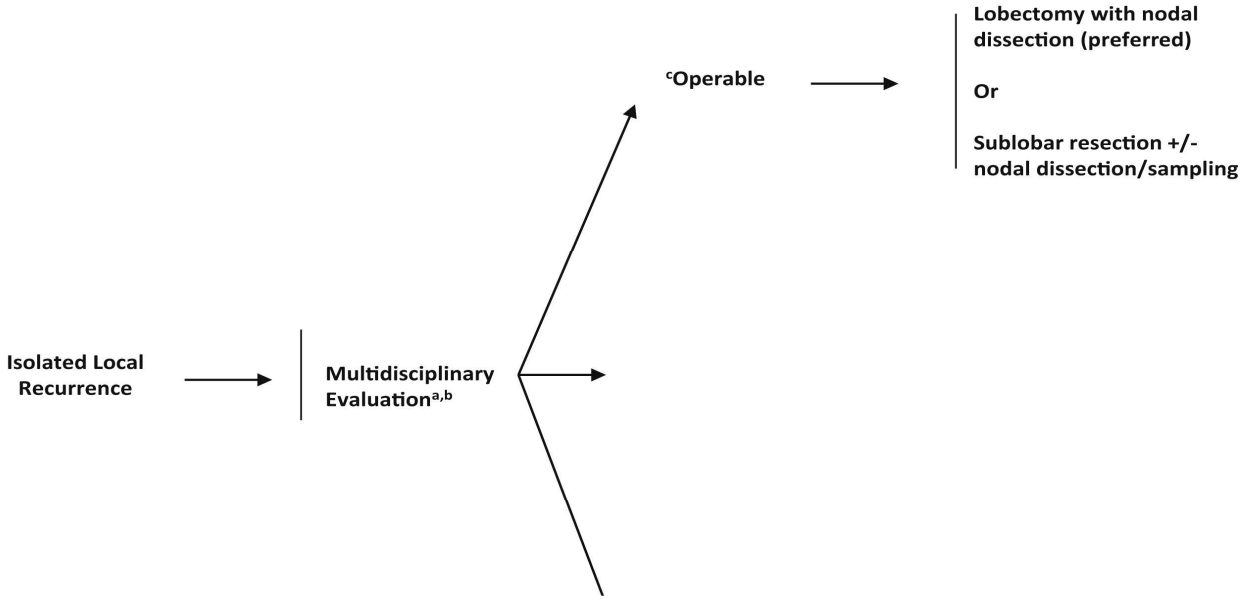


FIGURE 2. Meta-regression analysis showing the relationship between for re-SABR dose and survival (A), local control (B), and cumulative dose and toxicity (C). EQD2 indicates equivalent dose to 2 Gy; SABR, stereotactic ablative radiotherapy; SBRT, stereotactic body radiation therapy. full color online

Viani et al Am J Clin Oncol 2020

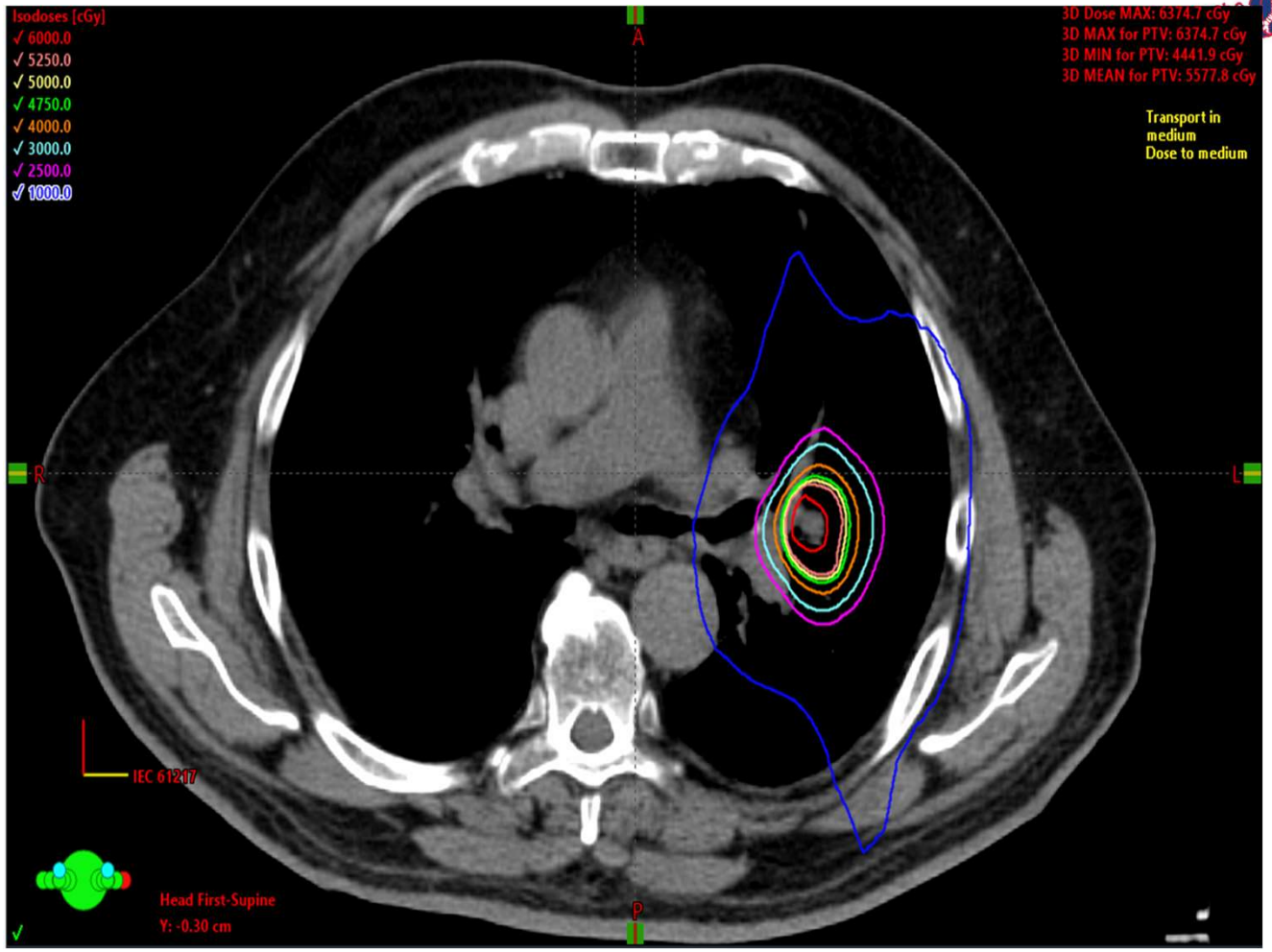
Suggested Treatment Algorithm



Kennedy WR, et al. Radioth Oncol 2020

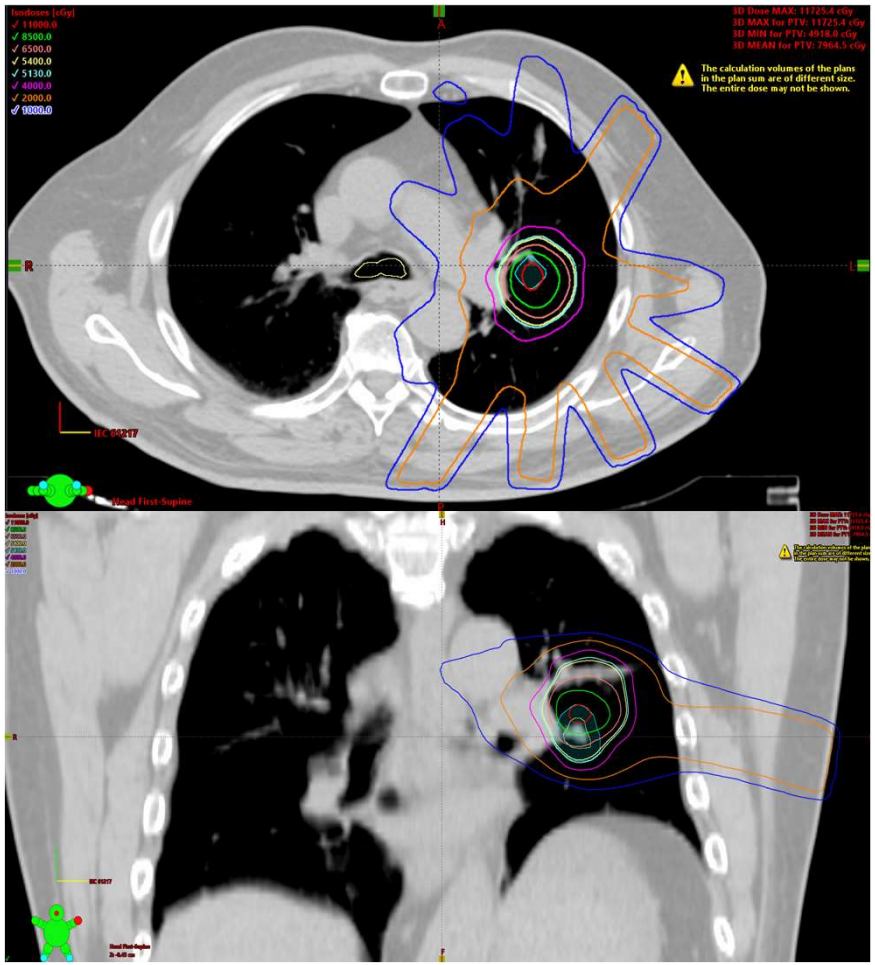
Case: Second Treatment

- Received 50 Gy in 5 fx delivered once daily
- VMAT 2 arcs: 175 to 345 degrees clockwise and counter clockwise
- Max dose 63.7 Gy located in GTV
- PBT max 37 Gy
- Pulmonary artery max 59 Gy
- Esophagus max 8 Gy
- Heart max 7 Gy



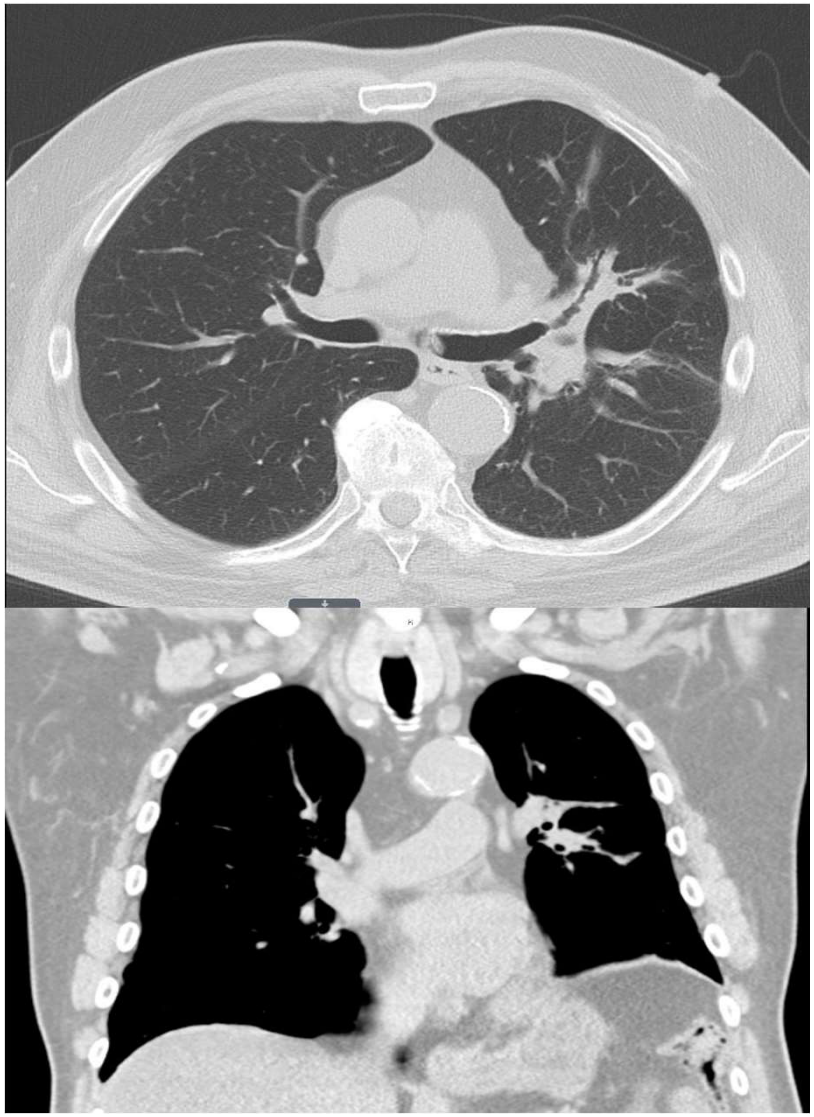
Case: Cumulative Radiation Plan

- Cumulative Max 117 Gy in lung parenchyma
- PBT max 50 Gy
  - No overlap on PBT
- Pulmonary artery max 70 Gy
- Esophagus max 11 Gy
- Heart max 14 Gy
- Cord max 9 Gy



Case: Patient Follow-up

- Now 3.5 years out from second course of SBRT
- Post-radiation fibrosis in LUL
- Asymptomatic
- No evidence of recurrent colon cancer or lung cancer



Future Directions

- Ideal fractionation scheme
- Development of validated dose constraints
- Utility of advanced technologies
  - Proton Therapy
  - MRI-guided SBRT
- Role of systemic therapies with SBRT

Key Points

- Multidisciplinary discussion crucial
- Tumor size and cumulative dose associated with toxicity
  - Local control associated with total dose
- Risk rises with cumulative EQD2 > 145 Gy
  - Create cumulative plan to evaluate dose to OARs
- Balance the benefit of treatment with risk of toxicity
  - Grade 3+ toxicity rate approx. 10%

Resources

- Viani GA, et al. Effectiveness and Safety of Reirradiation with Stereotactic Ablative Radiotherapy of Lung Cancer After a First Course of Thoracic Radiation. A Meta-analysis. Am J Clin Oncol 2020;43(8)575-581.
- Kennedy WR, et al. Repeat stereotactic body radiation therapy (SBRT) for salvage of isolated local recurrence after definitive lung SBRT. Radiother and Oncol. 2020;142,230-235
- Hearn JWD, et al. Salvage Stereotactic Body Radiation Therapy (SBRT) for Local Failure After Primary Lung SBRT. In J Radiat Oncol Biol Phys 2014;90(2)402-406.
- Peulen H, et al. Toxicity after reirradiation of pulmonary tumours with stereotactic body radiotherapy. Radiother Oncol 2011;101(2)260-266
- De Ruysscher D, et al. High-dose re-irradiation following radical radiotherapy for non-small-cell lung cancer. Lancet Oncol 2014;15(13)E620-E624

Early-Stage NSCLC with ILD

David Palma, MD, PhD, FRCPC
Professor, Western University
Clinician Scientist, Ontario Institute for Cancer Research

IASLC
INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

Case Presentation

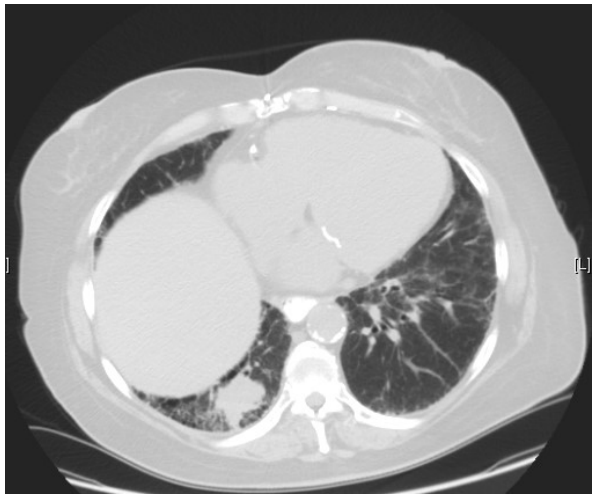
- 67 year old woman presents with a new, growing nodule in the right lower lobe.

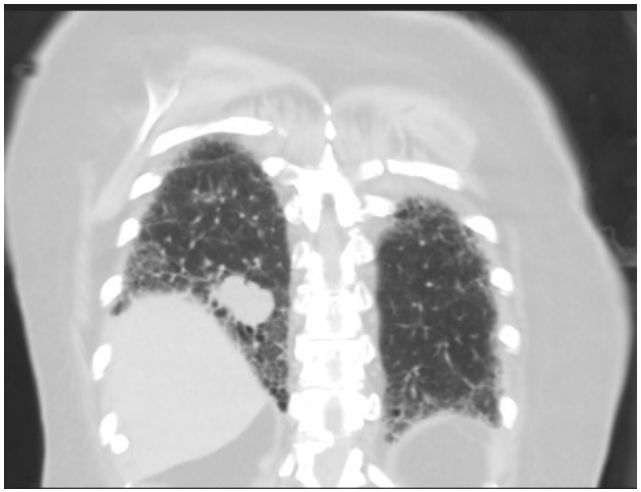
- She has a history of idiopathic pulmonary fibrosis diagnosed five years prior, and is dyspneic with any activity but not yet on oxygen. Prednisone-dependent at 15 mg daily.

- Med Hx: also CAD, MR, PVD with bypass, DM II, HTN, pulmonary hypertension

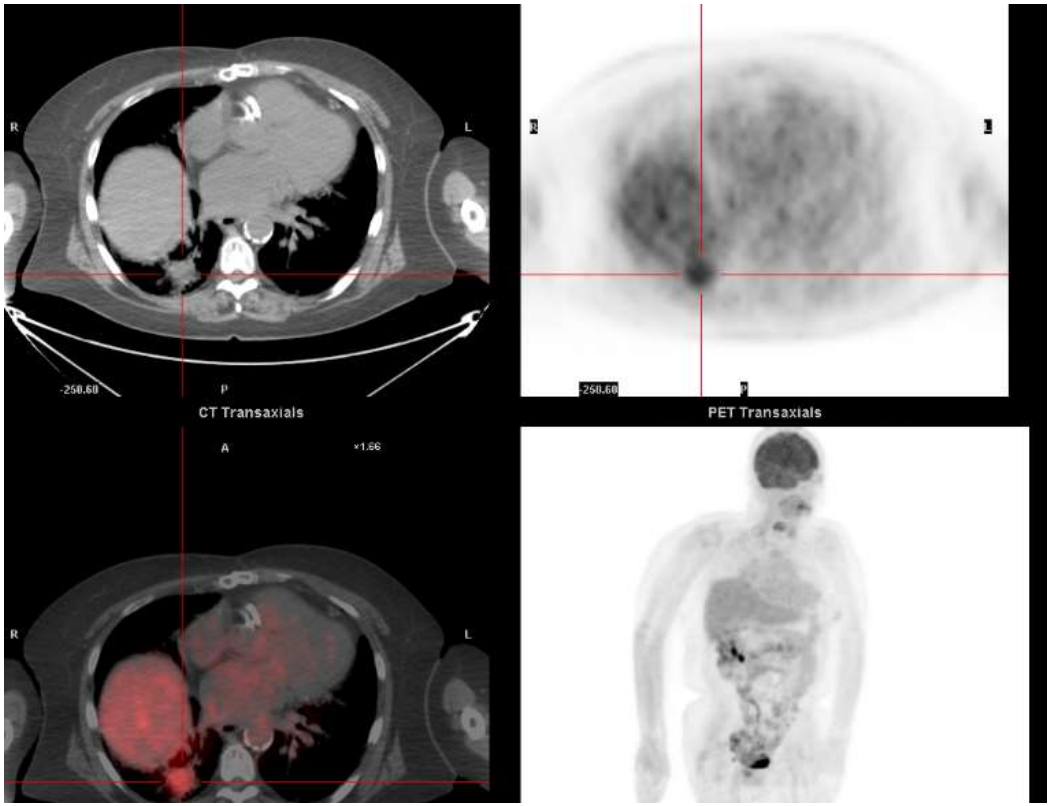
Investigations

- The nodule was detected incidentally on CT chest 6 months ago, measuring 3.2 cm in size, growing to 3.5 cm in size on repeat scan 3 months ago





PET/CT: SUVmax 3.2



Investigations

- CT-guided lung biopsy shows adenocarcinoma.
- PFTs: FEV1=101% predicted; DLCO/VA: 55%
- Brain imaging negative

Physical Exam

- Looks her staged age, not dyspneic at rest, but dyspneic getting to the exam table
- No lymphadenopathy palpable
- Bibasilar crackles on ausculation
- No other pertinent findings

Polling Question 5

Which treatment option would you recommend?

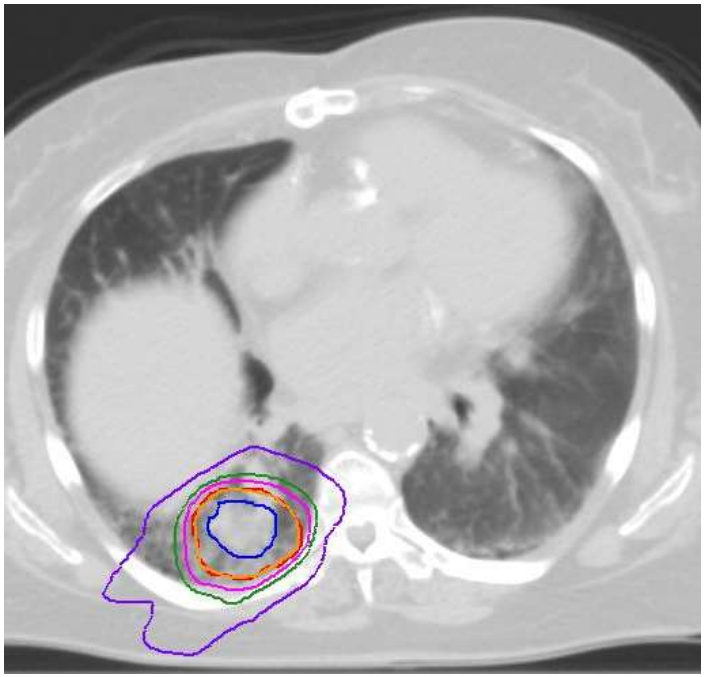
A. Surgical resection
B. SABR
C. Thermal ablation
D. Systemic therapy
E. Observation

Treatment

- PFTs were acceptable for resection but in the context of other co-morbidities, surgeon advised non-operative managment

- Consented to treatment with SABR, aware of potential increased risk of pulmonary toxicity due to ILD

- Treatment given as 60 Gy in 8 fractions



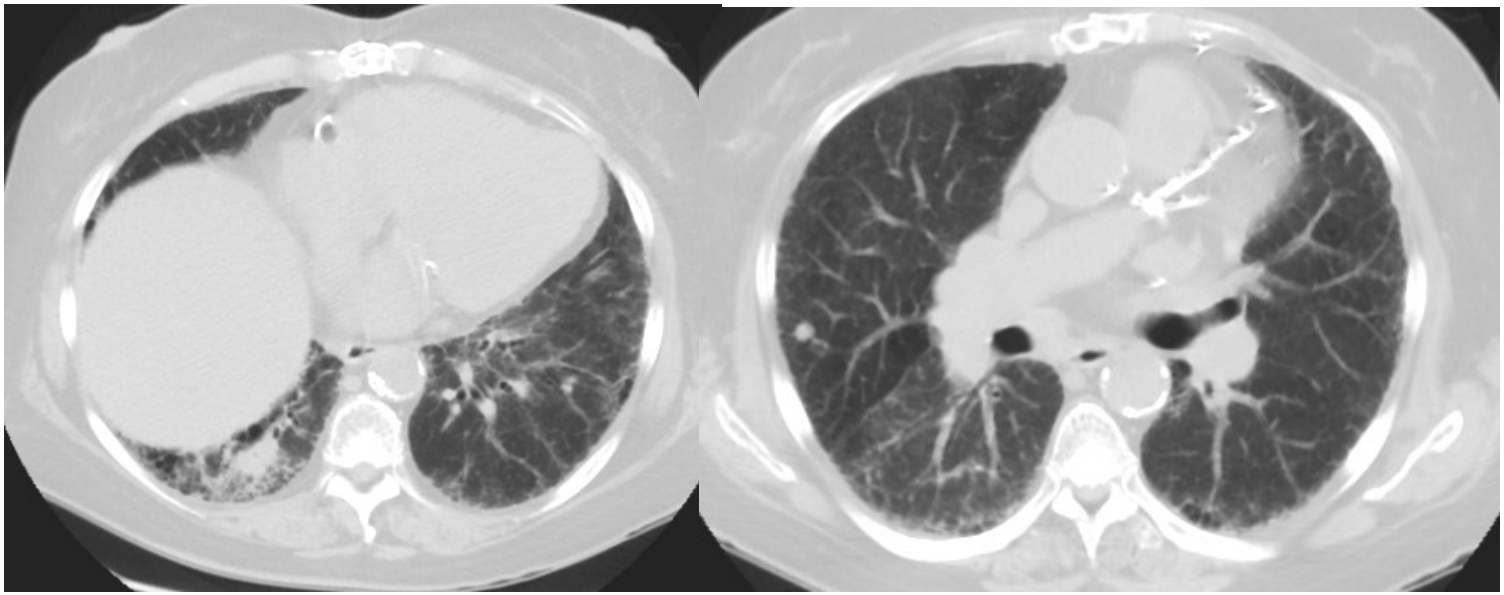
Follow-up

- Followed by Resp, Rad Onc, Vascular, Nephrology

- 0-3 months post-treatment:
  - No change in respiratory status
  - Fatigue

- 3 Month CT:
  - Lesion now 2.1 cm, surrounding post-radiation change
  - New nodules in RML measuring 6 and 8 mm
  - Right hilar fullness

3 month scans

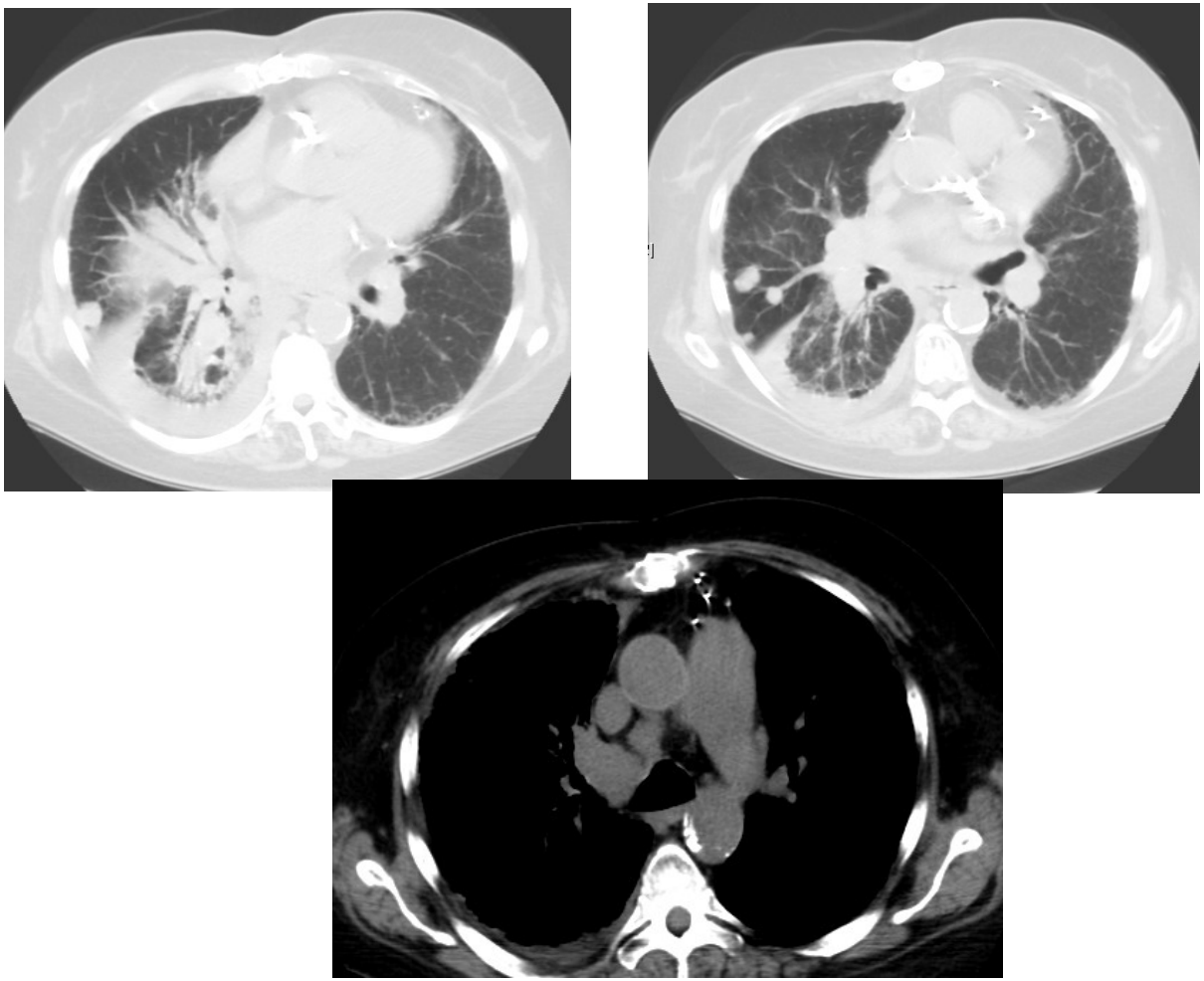


Follow-up

- 4-months post-treatment: febrile, chest pain, SOB
  - Treated with clarithromycin, improved back to baseline

- 9 months post-treatment
  - Exacerbation of ILD requiring admission, levofloxacin, prednisone 50 mg daily
  - Initiation of oxygen: remained oxygen dependent for life

CT: 1 yr post-treatment



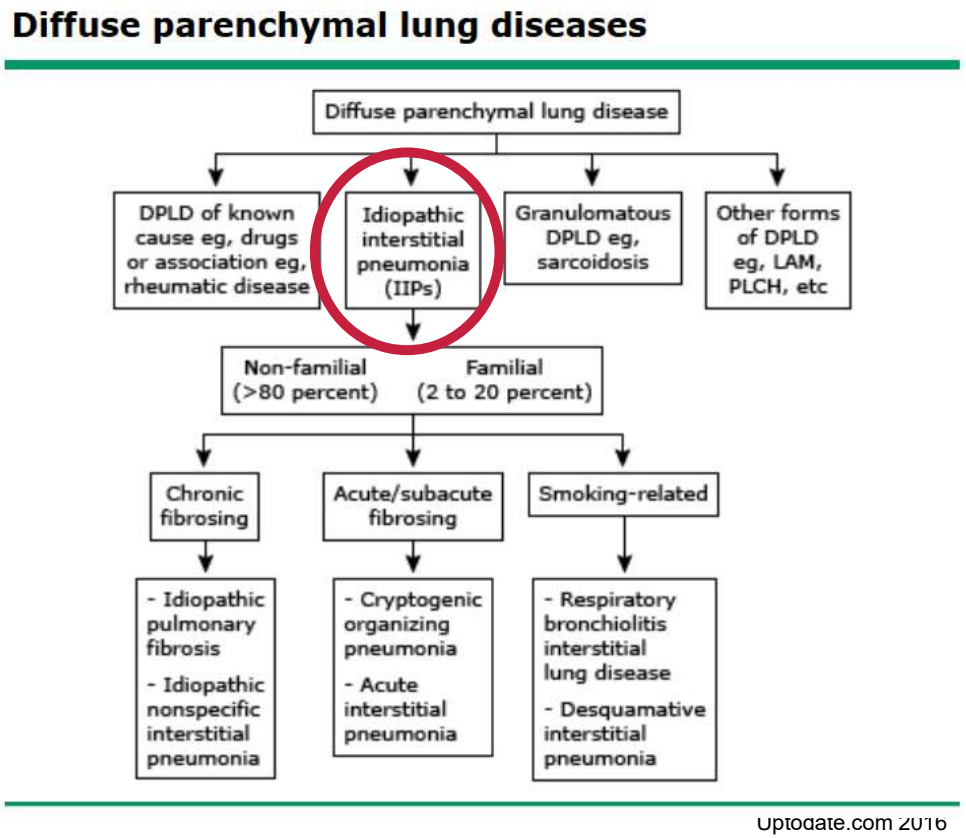
Subsequent follow-up

- Recurrent pneumonias and ILD exacerbations, interfering with ADLs
- Progressive intrathoracic metastatic disease
- Not eligible for cytotoxic chemotherapy, EGFR-negative

- Symptom management by palliative care team

ILD: A confusing collection of diseases

ILD is a large collection of lung diseases, also called diffuse parenchymal lung disease



ILD Classification

Journal of Thoracic Oncology

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REVIEW ARTICLE | VOLUME 15, ISSUE 6, P902-913, JUNE 01, 2020

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A Primer on Interstitial Lung Disease and Thoracic Radiation

Christopher D. Goodman, MD • Suzan F.M. Nijman, MD • Suresh Senan, MRCP, FRCR, PhD • Esther J. Nossent, MD • Christopher J. Ryerson, MD, FRCPC • Inderdeep Dhaliwal, MD, FRCPC • X. Melody Qu, MD, FRCPC • Joanna Laba, MD, FRCPC • George B. Rodrigues, MD, PhD, FRCPC, FASTRO • David A. Palma, MD, PhD, FRCPC •

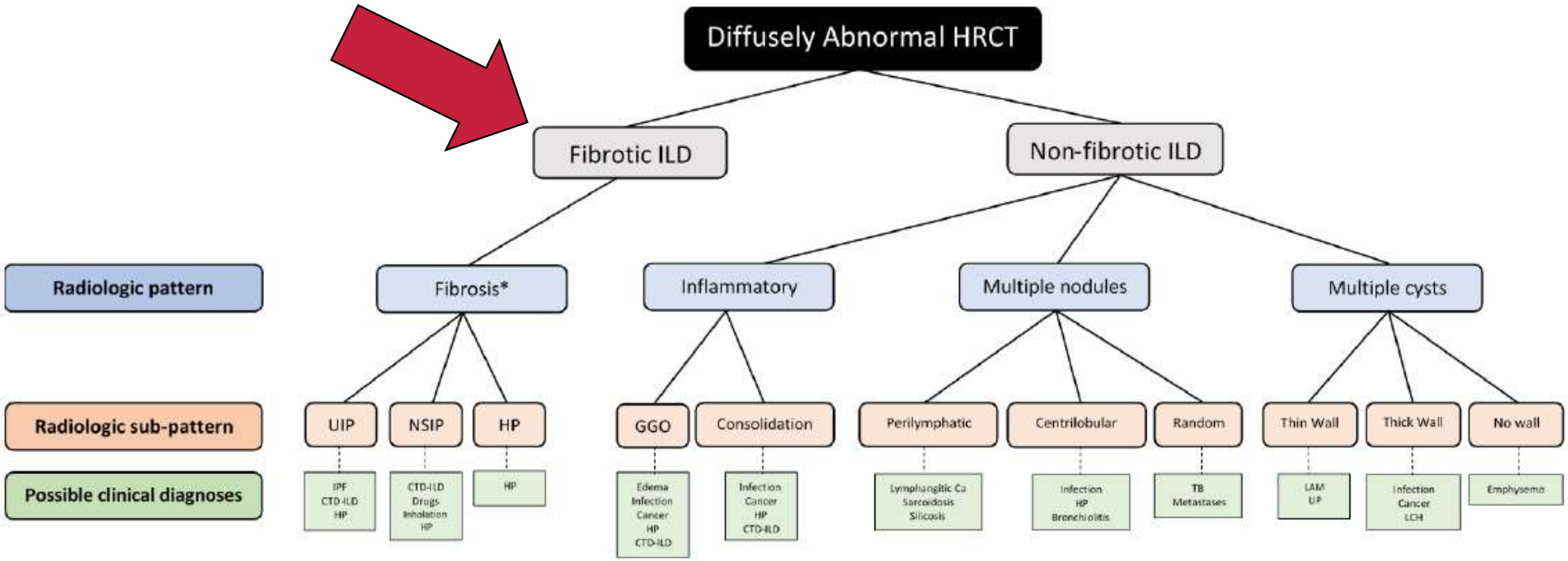
on behalf of the International Association for the Study of Lung Cancer Advanced Radiation Technology Committee •

Show less

Published: February 24, 2020 • DOI: https://doi.org/10.1016/j.jtho.2020.02.005 •

Check for updates

ILD Classification

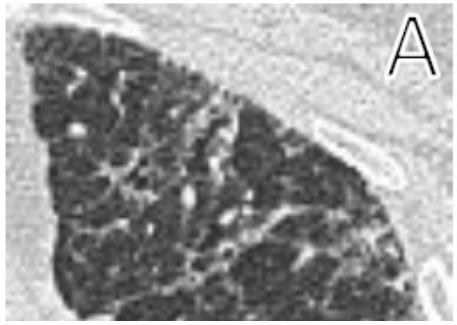


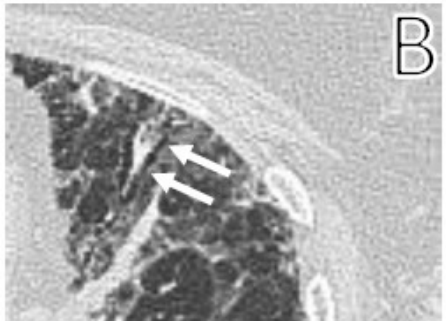
Fibrotic ILDs

- Idiopathic pulmonary fibrosis (IPF)
  - Honeycombing!!
- Connective tissue disease related
  - e.g. lupus, scleroderma
- Hypersensitivity pneumonitis
  - bird-fancier's lung
- Drug-induced
- Pneumoconioses
  - silica,asbestos
- Other/unclassified

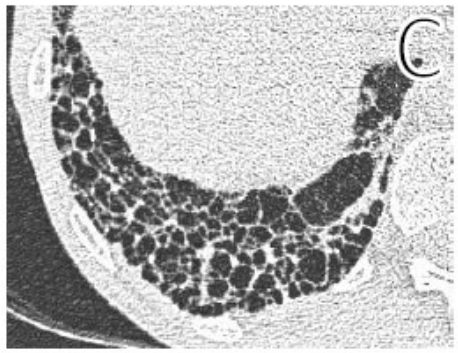
CT Findings

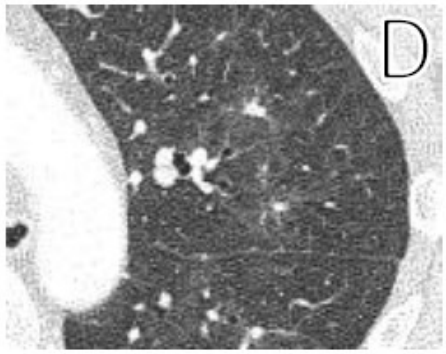
reticulation





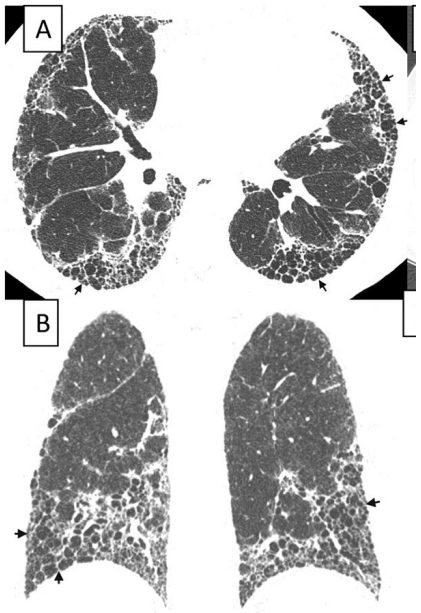
traction bronchiectasis





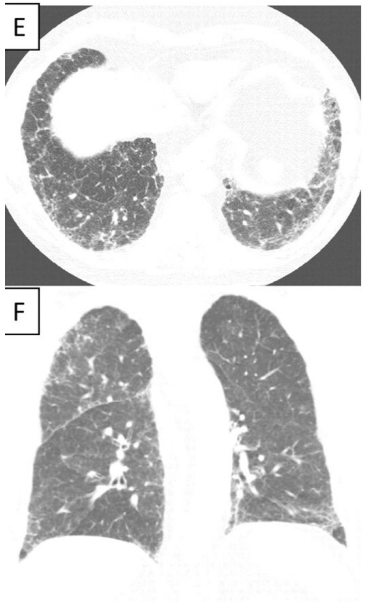
patchy GGO

Idiopathic Pulmonary Fibrosis



IPF is a chronic, progressive fibrotic interstitial lung disease of unknown origin

HRCT images: usual interstitial pneumonia (UIP) pattern



UIP pattern, with extensive honeycombing: basal predominant, peripheral predominant reticular abnormality, with multiple layers of honeycombing.

Possible UIP pattern; peripheral predominant, basal predominant reticular abnormality with moderate amount of ground glass abnormality, but without honeycombing.

ILD and SABR Systematic Review

Critical Review

Treatment-Related Toxicity in Patients With Early-Stage Non-Small Cell Lung Cancer and Coexisting Interstitial Lung Disease: A Systematic Review

Hanbo Chen, MD,* Suresh Senan, MRCP, FRCR, PhD,†
Esther J. Nossent, MD,‡ R. Gabriel Boldt, RLIS,* Andrew Warner, MSc,*
David A. Palma, MD, PhD, FRCPC,* and
Alexander V. Louie, MD, PhD, FRCPC*

*Department of Radiation Oncology, London Health Sciences Centre, London, Ontario, Canada, and Departments of †Radiation Oncology and ‡Pulmonology, VU University Medical Center, Amsterdam, The Netherlands

Group	Mortality	Toxicity
All ILD subtypes	15.6%	25%
IPF only studies	33%	71%

Chen H, Senan S, Nossent EJ, et al. Treatment-Related Toxicity in Patients With Early-Stage Non-Small Cell Lung Cancer and Coexisting Interstitial Lung Disease: A Systematic Review. *Int J Radiat Oncol Biol Phys.* 2017;98(3):622-631. doi:10.1016/j.ijrobp.2017.03.010

ILD and Surgery

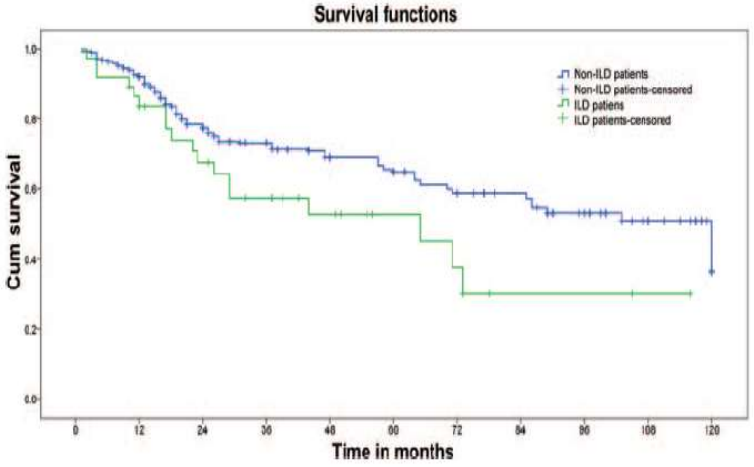
Impact of interstitial lung disease on short-term and long-term survival of patients undergoing surgery for non-small-cell lung cancer: analysis of risk factors†

Luca Voltolini[a,*], Stefano Bongiolatti[a], Luca Luzzi[a], Elena Bargagli[b], Antonella Fossi[b], Claudia Ghiribelli[a], Paola Rottoli[b] and Giuseppe Gotti[a]

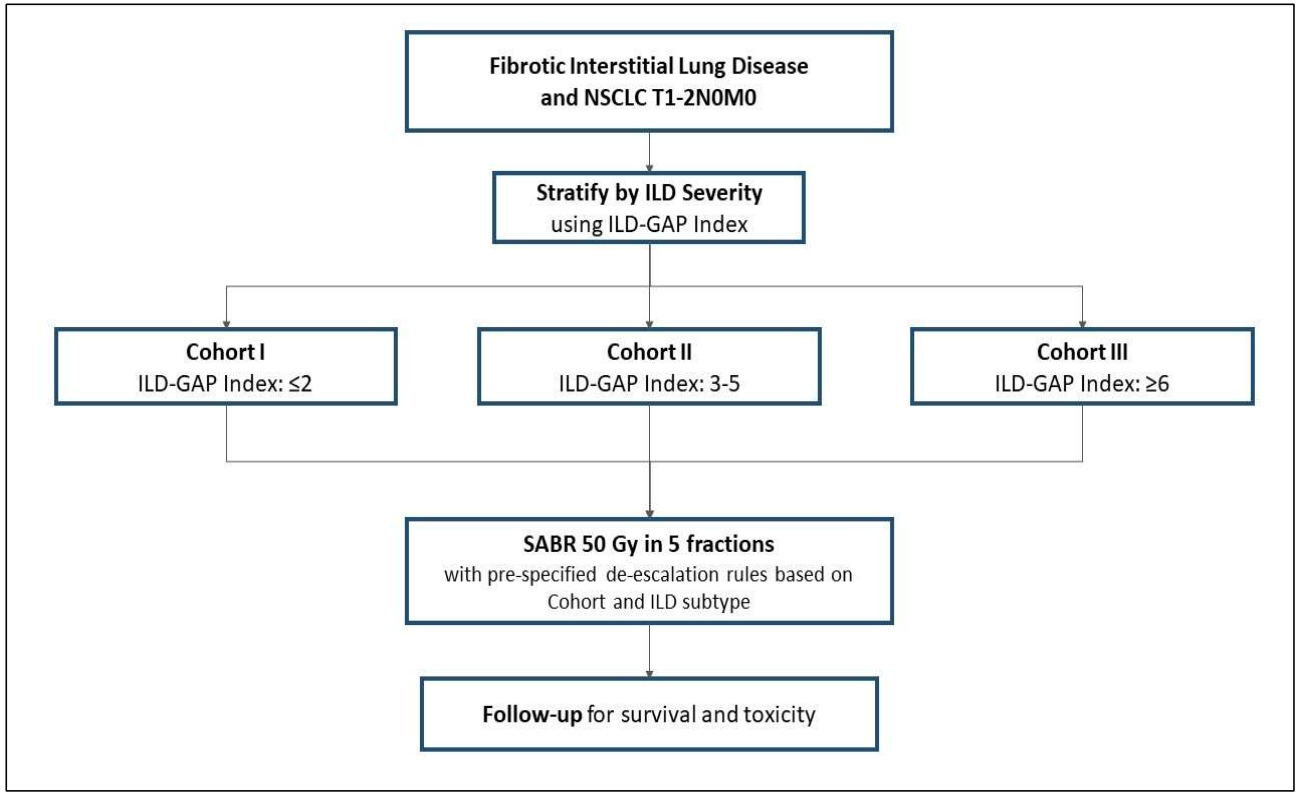
Table 3: Procedure-specific mortality and incidence of ARDS/ALI after pulmonary resection

	ILD group ($n = 37$)	Non-ILD group ($n = 738$)	P-value
Mean hospital stay	12.51 ± 5.5	9.58 ± 4.1	≤0.01
Total deaths	3 (8.1%)	10 (1.4%)	≤0.01
Pneumonectomy	1/4 (25%)	3/90 (3.3%)	
Lobectomy	2/30 (6.6%)	7/528 (1.3%)	
Sublobar resection	0/3	0/114	
ARDS/ALI	5 (13.5%)	17 (2.3%)	≤0.01
Pneumonectomy	1/4 (25%)	7/90 (7.8%)	
Lobectomy	3/30 (10%)	8/528 (1.5%)	
Sublobar resection	1/3 (33%)	2/114 (1.8%)	

ILD: interstitial lung disease; ARDS: acute respiratory disease syndrome; ALI: acute lung injury.



Voltolini L, Bongiolatti S, Luzzi L, et al. Impact of interstitial lung disease on short-term and long-term survival of patients undergoing surgery for non-small-cell lung cancer: analysis of risk factors. *Eur J Cardiothorac Surg*. 2013;43(1):e17-e23. doi:10.1093/ejcts/ezs560



The ILD-GAP Model

Chest 2014; 145(4):723-28

	Predictor	Points
ILD	ILD subtype	
	IPF	0
	Unclassifiable ILD	0
	CT-ILD/idiopathic NSIP	-2
	Chronic HP	-2
G	Gender	
	Female	0
	Male	1
A	Age, yr	
	≤ 60	0
	61-65	1
	> 65	2
P	Physiology	
	FVC, % predicted	
	> 75%	0
	50-75%	1
	<50%	2
	DLCO, % predicted	
	> 55%	0
	36-55%	1
	≤ 35%	2
	Cannot perform	3
	Total possible points	**8**

Palma DA, Chen H, Bahig H, et al. Assessment of precision irradiation in early non-small cell lung cancer and interstitial lung disease (ASPIRE-ILD): study protocol for a phase II trial. *BMC Cancer*. 2019;19(1):1206. Published 2019 Dec 11. doi:10.1186/s12885-019-6392-8

ILD and SABR

- Many consider ILD and IPF a **relative** contraindication to SABR, but alternative options may be limited
- In this scenario, multidisciplinary opinion is required, with careful discussion with the patient
- Options:
  - SABR: as gentle a dose as possible
  - Observe (if life expectancy short)
  - Systemic therapies

Take Home Messages

- The management of lung cancer in the setting of ILD is challenging
- Surgical resection preferred if adequate pulmonary reserve
- If not surgery, then approach will depend on patient & tumor board consideration of relative risks of treatment vs. untreated lung cancer